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(54) Title: CORYNEBACTERIUM GLUTAMICUM GENES ENCODING STRESS, RESISTANCE AND TOLERANCE PROTEINS

(57) Abstract: Isolated nucleic acid molecules, designated SRT nucleic acid molecules, which encode novel SRT proteins from Corynebacterium glutamicum are described. The invention also provides antisense nucleic acid molecules, recombinant expression vectors containing SRT nucleic acid molecules, and host cells into which the expression vectors have been introduced. The invention still further provides isolated SRT proteins, mutated SRT proteins, fusion proteins, antigenic peptides and methods for the improvement of production of a desired compound from C. glutamicum based on genetic engineering of SRT genes in this organism.



CORYNEBACTERIUM GLUTAMICUM GENES ENCODING STRESS, RESISTANCE AND TOLERANCE PROTEINS

Related Applications

This application claims priority to prior filed U.S. Provisional Patent Application Serial No. 60/141031, filed June 25, 1999, U.S. Provisional Patent Application Serial No. 60/142692, filed July 1, 1999, and also to U.S. Provisional Patent Application Serial No. 60/151214, filed August 27, 1999. This application also claims priority to German Patent Application No. 19930429.7, filed July 1, 1999, German Patent Application No. 19931457.8, filed July 8, 1999, German Patent Application No. 19931457.8, filed July 8, 1999, German Patent Application No. 19932230.9, filed July 9, 1999, German Patent Application No. 19932230.9, filed July 9, 1999, German Patent Application No. 19932214.1, filed July 14, 1999, German Patent Application No. 19940764.9, filed August 27, 1999, and German Patent Application No. 19941382.7, filed August 31, 1999. The entire contents of all of the aforementioned applications are hereby expressly incorporated herein in their entirety by this reference.

Background of the Invention

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Certain products and by-products of naturally-occurring metabolic processes in cells have utility in a wide array of industries, including the food, feed, cosmetics, and pharmaceutical industries. These molecules, collectively termed 'fine chemicals', include organic acids, both proteinogenic and non-proteinogenic amino acids, nucleotides and nucleosides, lipids and fatty acids, diols, carbohydrates, aromatic compounds, vitamins and cofactors, and enzymes. Their production is most conveniently performed through large-scale culture of bacteria developed to produce and secrete large quantities of a particular desired molecule. One particularly useful organism for this purpose is *Corynebacterium glutamicum*, a gram positive, nonpathogenic bacterium. Through strain selection, a number of mutant strains have been developed which produce an array of desirable compounds. However, selection of strains improved for the production of a particular molecule is a time-consuming and difficult process.

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Summary of the Invention

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The invention provides novel bacterial nucleic acid molecules which have a variety of uses. These uses include the identification of microorganisms which can be used to produce fine chemicals, the modulation of fine chemical production in *C. glutamicum* or related bacteria, the typing or identification of *C. glutamicum* or related bacteria, as reference points for mapping the *C. glutamicum* genome, and as markers for transformation. These novel nucleic acid molecules encode proteins, referred to herein as stress, resistance and tolerance (SRT) proteins.

C. glutamicum is a gram positive, aerobic bacterium which is commonly used in industry for the large-scale production of a variety of fine chemicals, and also for the degradation of hydrocarbons (such as in petroleum spills) and for the oxidation of terpenoids. The SRT nucleic acid molecules of the invention, therefore, can be used to identify microorganisms which can be used to produce fine chemicals, e.g., by fermentation processes. Modulation of the expression of the SRT nucleic acids of the invention, or modification of the sequence of the SRT nucleic acid molecules of the invention, can be used to modulate the production of one or more fine chemicals from a microorganism (e.g., to improve the yield or production of one or more fine chemicals from a Corynebacterium or Brevibacterium species).

The SRT nucleic acids of the invention may also be used to identify an organism as being Corynebacterium glutamicum or a close relative thereof, or to identify the presence of C. glutamicum or a relative thereof in a mixed population of microorganisms. The invention provides the nucleic acid sequences of a number of C. glutamicum genes; by probing the extracted genomic DNA of a culture of a unique or mixed population of microorganisms under stringent conditions with a probe spanning a region of a C. glutamicum gene which is unique to this organism, one can ascertain whether this organism is present. Although Corynebacterium glutamicum itself is nonpathogenic, it is related to species pathogenic in humans, such as Corynebacterium diphtheriae (the causative agent of diphtheria); the detection of such organisms is of significant clinical relevance.

The SRT nucleic acid molecules of the invention may also serve as reference points for mapping of the *C. glutamicum* genome, or of genomes of related organisms.

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Similarly, these molecules, or variants or portions thereof, may serve as markers for genetically engineered Corynebacterium or Brevibacterium species.

The SRT proteins encoded by the novel nucleic acid molecules of the invention are capable of, for example, permitting C. glutamicum to survive in a setting which is either chemically or environmentally hazardous to this microorganism. Given the availability of cloning vectors for use in Corynebacterium glutamicum, such as those disclosed in Sinskey et al., U.S. Patent No. 4,649,119, and techniques for genetic manipulation of C. glutamicum and the related Brevibacterium species (e.g., lactofermentum) (Yoshihama et al., J. Bacteriol. 162: 591-597 (1985); Katsumata et al., J. Bacteriol. 159: 306-311 (1984); and Santamaria et al., J. Gen. Microbiol. 130: 2237-2246 (1984)), the nucleic acid molecules of the invention may be utilized in the genetic engineering of this organism to make it a better or more efficient producer of one or more fine chemicals, through the ability of these proteins to permit growth and multiplication of C. glutamicum (and also continuous production of one or more fine chemicals) under circumstances which would normally impede growth of the organism, such as those conditions frequently encountered during large-scale fermentative growth. For example, by overexpressing or engineering a heat-shock induced protease molecule such that it is optimized in activity, one may increase the ability of the bacterium to degrade incorrectly folded proteins when the bacterium is challenged with high temperatures. By having fewer misfolded (and possibly misregulated or nonfunctional) 20 proteins to interfere with normal reaction mechanisms in the cell, the cell is increased in its ability to function normally in such a culture, which should in turn provide increased viability. This overall increase in number of cells having greater viability and activity in the culture should also result in an increase in yield, production, and/or efficiency of production of one or more desired fine chemicals, due at least to the relatively greater number of cells producing these chemicals in the culture.

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This invention provides novel SRT nucleic acid molecules which encode SRT proteins which are capable of, for example, permitting C. glutamicum to survive in a setting which is either chemically or environmentally hazardous to this microorganism. Nucleic acid molecules encoding an SRT protein are referred to herein as SRT nucleic acid molecules. In a preferred embodiment, the SRT protein participates in metabolic pathways permitting C. glutamicum to survive in a setting which is either chemically or

environmentally hazardous to this microorganism. Examples of such proteins include those encoded by the genes set forth in Table 1.

Accordingly, one aspect of the invention pertains to isolated nucleic acid molecules (e.g., cDNAs, DNAs, or RNAs) comprising a nucleotide sequence encoding an SRT protein or biologically active portions thereof, as well as nucleic acid fragments suitable as primers or hybridization probes for the detection or amplification of SRTencoding nucleic acid (e.g., DNA or mRNA). In particularly preferred embodiments, the isolated nucleic acid molecule comprises one of the nucleotide sequences set forth as the odd-numbered SEQ ID NOs in the Sequence Listing (e.g., SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7....), or the coding region or a complement thereof of one of these nucleotide sequences. In other particularly preferred embodiments, the isolated nucleic acid molecule of the invention comprises a nucleotide sequence which hybridizes to or is at least about 50%, preferably at least about 60%, more preferably at least about 70%, 80% or 90%, and even more preferably at least about 95%, 96%, 97%, 98%, 99% or more homologous to a nucleotide sequence set forth as an odd-numbered SEQ ID NO in the Sequence Listing (e.g., SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7...), or a portion thereof. In other preferred embodiments, the isolated nucleic acid molecule encodes one of the amino acid sequences set forth as an evennumbered SEQ ID NO in the Sequence Listing (e.g., SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8...).. The preferred SRT proteins of the present invention also preferably possess at least one of the SRT activities described herein.

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In another embodiment, the isolated nucleic acid molecule encodes a protein or portion thereof wherein the protein or portion thereof includes an amino acid sequence which is sufficiently homologous to an amino acid sequence of the invention (e.g., a sequence having an even-numbered SEQ ID NO: in the Sequence Listing), e.g., sufficiently homologous to an amino acid sequence of the invention such that the protein or portion thereof maintains an SRT activity. Preferably, the protein or portion thereof encoded by the nucleic acid molecule maintains the ability to increase the survival of *C. glutamicum* in a setting which is either chemically or environmentally hazardous to this microorganism. In one embodiment, the protein encoded by the nucleic acid molecule is at least about 50%, preferably at least about 60%, and more preferably at least about 70%, 80%, or 90% and most preferably at least about 95%, 96%, 97%, 98%, or 99% or

more homologous to an amino acid sequence of the invention (e.g., an entire amino acid sequence selected from those having an even-numbered SEQ ID NO in the Sequence Listing). In another preferred embodiment, the protein is a full length *C. glutamicum* protein which is substantially homologous to an entire amino acid sequence of the invention (encoded by an open reading frame shown the corresponding odd-numbered SEQ ID NOs in the Sequence Listing (e.g., SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7....).

In another preferred embodiment, the isolated nucleic acid molecule is derived from *C. glutamicum* and encodes a protein (*e.g.*, an SRT fusion protein) which includes a biologically active domain which is at least about 50% or more homologous to one of the amino acid sequences of the invention (*e.g.*, a sequence of one of the even-numbered SEQ ID NOs in the Sequence Listing) and has the ability to increase the survival of *C. glutamicum* in a setting which is either chemically or environmentally hazardous to this microorganism, or possesses one or more of the activities set forth in Table 1, and which also includes heterologous nucleic acid sequences encoding a heterologous polypeptide or regulatory regions.

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In another embodiment, the isolated nucleic acid molecule is at least 15 nucleotides in length and hybridizes under stringent conditions to a nucleic acid molecule comprising a nucleotide sequence of the invention (e.g., a sequence of an odd-numbered SEQ ID NO in the Sequence Listing). Preferably, the isolated nucleic acid molecule corresponds to a naturally-occurring nucleic acid molecule. More preferably, the isolated nucleic acid encodes a naturally-occurring C. glutamicum SRT protein, or a biologically active portion thereof.

Another aspect of the invention pertains to vectors, e.g., recombinant expression vectors, containing the nucleic acid molecules of the invention, and host cells into which such vectors have been introduced. In one embodiment, such a host cell is used to produce an SRT protein by culturing the host cell in a suitable medium. The SRT protein can be then isolated from the medium or the host cell.

Yet another aspect of the invention pertains to a genetically altered microorganism in which an SRT gene has been introduced or altered. In one embodiment, the genome of the microorganism has been altered by the introduction of a nucleic acid molecule of the invention encoding wild-type or mutated SRT sequence as

a transgene. In another embodiment, an endogenous SRT gene within the genome of the microorganism has been altered, e.g., functionally disrupted, by homologous recombination with an altered SRT gene. In another embodiment, an endogenous or introduced SRT gene in a microorganism has been altered by one or more point

5 mutations, deletions, or inversions, but still encodes a functional SRT protein. In still another embodiment, one or more of the regulatory regions (e.g., a promoter, repressor, or inducer) of a SRT gene in a microorganism has been altered (e.g., by deletion, truncation, inversion, or point mutation) such that the expression of the SRT gene is modulated. In a preferred embodiment, the microorganism belongs to the genus

10 Corynebacterium or Brevibacterium, with Corynebacterium glutamicum being particularly preferred. In a preferred embodiment, the microorganism is also utilized for the production of a desired compound, such as an amino acid, with lysine being particularly preferred.

In another aspect, the invention provides a method of identifying the presence or activity of *Cornyebacterium diphtheriae* in a subject. This method includes detection of one or more of the nucleic acid or amino acid sequences of the invention (e.g., the sequences set forth in the Sequence Listing as SEQ ID NOs 1 through 304)) in a subject, thereby detecting the presence or activity of *Corynebacterium diphtheriae* in the subject.

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Still another aspect of the invention pertains to an isolated SRT protein or a portion, e.g., a biologically active portion, thereof. In a preferred embodiment, the isolated SRT protein or portion thereof possesses the ability to increase the survival of C. glutamicum in a setting which is either chemically or environmentally hazardous to this microorganism. In another preferred embodiment, the isolated SRT protein or portion thereof is sufficiently homologous to an amino acid sequence of the invention (e.g., a sequence of an even-numbered SEQ ID NO: in the Sequence Listing) such that the protein or portion thereof maintains the ability to increase the survival of C. glutamicum in a setting which is either chemically or environmentally hazardous to this microorganism.

The invention also provides an isolated preparation of an SRT protein. In preferred embodiments, the SRT protein comprises an amino acid sequence of the invention (e.g., a sequence of an even-numbered SEQ ID NO: of the Sequence Listing). In another preferred embodiment, the invention pertains to an isolated full length protein

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which is substantially homologous to an entire amino acid sequence of the invention (e.g., a sequence of an even-numbered SEQ ID NO: of the Sequence Listing) (encoded by an open reading frame set forth in a corresponding odd-numbered SEQ ID NO: of the Sequence Listing).). In yet another embodiment, the protein is at least about 50%, preferably at least about 60%, and more preferably at least about 70%, 80%, or 90%, and most preferably at least about 95%, 96%, 97%, 98%, or 99% or more homologous to an entire amino acid sequence of the invention (e.g., a sequence of an even-numbered SEQ ID NO: of the Sequence Listing). In other embodiments, the isolated SRT protein comprises an amino acid sequence which is at least about 50% or more homologous to one of the amino acid sequences of the invention (e.g., a sequence of an even-numbered SEQ ID NO: of the Sequence Listing) and is able to improve the survival rate of C. glutamicum in a setting which is either chemically or environmentally hazardous to this microorganism, or has one or more of the activities set forth in Table 1.

Alternatively, the isolated SRT protein can comprise an amino acid sequence which is encoded by a nucleotide sequence which hybridizes, e.g., hybridizes under stringent conditions, or is at least about 50%, preferably at least about 60%, more preferably at least about 70%, 80%, or 90%, and even more preferably at least about 95%, 96%, 97%, 98,%, or 99% or more homologousto a nucleotide sequence of one of the even-numbered SEQ ID NOs set forth in the Sequence Listing. It is also preferred that the preferred forms of SRT proteins also have one or more of the SRT bioactivities described herein.

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The SRT polypeptide, or a biologically active portion thereof, can be operatively linked to a non-SRT polypeptide to form a fusion protein. In preferred embodiments, this fusion protein has an activity which differs from that of the SRT protein alone. In other preferred embodiments, this fusion protein results in increased yields, production, and/or efficiency of production of a desired fine chemical from *C. glutamicum*. In particularly preferred embodiments, integration of this fusion protein into a host cell modulates the production of a desired compound from the cell.

In another aspect, the invention provides methods for screening molecules which modulate the activity of an SRT protein, either by interacting with the protein itself or a substrate or binding partner of the SRT protein, or by modulating the transcription or translation of an SRT nucleic acid molecule of the invention.

Another aspect of the invention pertains to a method for producing a fine chemical. This method involves the culturing of a cell containing a vector directing the expression of an SRT nucleic acid molecule of the invention, such that a fine chemical is produced. In a preferred embodiment, this method further includes the step of obtaining a cell containing such a vector, in which a cell is transfected with a vector directing the expression of an SRT nucleic acid. In another preferred embodiment, this method further includes the step of recovering the fine chemical from the culture. In a particularly preferred embodiment, the cell is from the genus *Corynebacterium* or *Brevibacterium*, or is selected from those strains set forth in Table 3.

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Another aspect of the invention pertains to methods for modulating production of a molecule from a microorganism. Such methods include contacting the cell with an agent which modulates SRT protein activity or SRT nucleic acid expression such that a cell associated activity is altered relative to this same activity in the absence of the agent. In a preferred embodiment, the cell is modulated in resistance to one or more toxic chemicals or in resistance to one or more environmental stresses, such that the yields or rate of production of a desired fine chemical by this microorganism is improved. The agent which modulates SRT protein activity can be an agent which stimulates SRT protein activity or SRT nucleic acid expression. Examples of agents which stimulate SRT protein activity or SRT nucleic acid expression include small molecules, active SRT proteins, and nucleic acids encoding SRT proteins that have been introduced into the cell. Examples of agents which inhibit SRT activity or expression include small molecules, and antisense SRT nucleic acid molecules.

Another aspect of the invention pertains to methods for modulating yields of a desired compound from a cell, involving the introduction of a wild-type or mutant SRT gene into a cell, either maintained on a separate plasmid or integrated into the genome of the host cell. If integrated into the genome, such integration can random, or it can take place by homologous recombination such that the native gene is replaced by the introduced copy, causing the production of the desired compound from the cell to be modulated. In a preferred embodiment, said yields are increased. In another preferred embodiment, said chemical is a fine chemical. In a particularly preferred embodiment, said fine chemical is an amino acid. In especially preferred embodiments, said amino acid is L-lysine.

Detailed Description of the Invention

The present invention provides SRT nucleic acid and protein molecules which are involved in the survival of *C. glutamicum* upon exposure of this microorganism to chemical or environmental hazards. The molecules of the invention may be utilized in the modulation of production of fine chemicals from microorganisms, since these SRT proteins provide a means for continued growth and multiplication of *C. glutamicum* in the presence of toxic chemicals or hazardous environmental conditions, such as may be encountered during large-scale fermentative growth. By increasing the growth rate or at least maintaining normal growth in the face of poor, if not toxic, conditions, one may increase the yield, production, and/or efficiency of production of one or more fine chemicals from such a culture, at least due to the relatively greater number of cells producing the fine chemical in the culture. Aspects of the invention are further explicated below.

15 I. Fine Chemicals

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The term 'fine chemical' is art-recognized and includes molecules produced by an organism which have applications in various industries, such as, but not limited to, the pharmaceutical, agriculture, and cosmetics industries. Such compounds include organic acids, such as tartaric acid, itaconic acid, and diaminopimelic acid, both 20 proteinogenic and non-proteinogenic amino acids, purine and pyrimidine bases, nucleosides, and nucleotides (as described e.g. in Kuninaka, A. (1996) Nucleotides and related compounds, p. 561-612, in Biotechnology vol. 6, Rehm et al., eds. VCH: Weinheim, and references contained therein), lipids, both saturated and unsaturated fatty acids (e.g., arachidonic acid), diols (e.g., propane diol, and butane diol), carbohydrates 25 (e.g., hyaluronic acid and trehalose), aromatic compounds (e.g., aromatic amines, vanillin, and indigo), vitamins and cofactors (as described in Ullmann's Encyclopedia of Industrial Chemistry, vol. A27, "Vitamins", p. 443-613 (1996) VCH: Weinheim and references therein; and Ong, A.S., Niki, E. & Packer, L. (1995) "Nutrition, Lipids, Health, and Disease" Proceedings of the UNESCO/Confederation of Scientific and 30 Technological Associations in Malaysia, and the Society for Free Radical Research – Asia, held Sept. 1-3, 1994 at Penang, Malaysia, AOCS Press, (1995)), enzymes, polyketides (Cane et al. (1998) Science 282: 63-68), and all other chemicals described in

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Gutcho (1983) Chemicals by Fermentation, Noyes Data Corporation, ISBN: 0818805086 and references therein. The metabolism and uses of certain of these fine chemicals are further explicated below.

5 A. Amino Acid Metabolism and Uses

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Amino acids comprise the basic structural units of all proteins, and as such are essential for normal cellular functioning in all organisms. The term "amino acid" is artrecognized. The proteinogenic amino acids, of which there are 20 species, serve as structural units for proteins, in which they are linked by peptide bonds, while the nonproteinogenic amino acids (hundreds of which are known) are not normally found in proteins (see Ulmann's Encyclopedia of Industrial Chemistry, vol. A2, p. 57-97 VCH; Weinheim (1985)). Amino acids may be in the D- or L- optical configuration, though Lamino acids are generally the only type found in naturally-occurring proteins. Biosynthetic and degradative pathways of each of the 20 proteinogenic amino acids have been well characterized in both prokaryotic and eukaryotic cells (see, for example, 15 Stryer, L. Biochemistry, 3rd edition, pages 578-590 (1988)). The 'essential' amino acids (histidine, isoleucine, leucine, lysine, methionine, phenylalanine, threonine, tryptophan, and valine), so named because they are generally a nutritional requirement due to the complexity of their biosyntheses, are readily converted by simple biosynthetic pathways. to the remaining 11 'nonessential' amino acids (alanine, arginine, asparagine, aspartate, cysteine, glutamate, glutamine, glycine, proline, serine, and tyrosine). Higher animals do retain the ability to synthesize some of these amino acids, but the essential amino acids must be supplied from the diet in order for normal protein synthesis to occur.

Aside from their function in protein biosynthesis, these amino acids are interesting chemicals in their own right, and many have been found to have various applications in the food, feed, chemical, cosmetics, agriculture, and pharmaceutical industries. Lysine is an important amino acid in the nutrition not only of humans, but also of monogastric animals such as poultry and swine. Glutamate is most commonly used as a flavor additive (mono-sodium glutamate, MSG) and is widely used throughout the food industry, as are aspartate, phenylalanine, glycine, and cysteine. Glycine, Lmethionine and tryptophan are all utilized in the pharmaceutical industry. Glutamine, valine, leucine, isoleucine, histidine, arginine, proline, serine and alanine are of use in

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both the pharmaceutical and cosmetics industries. Threonine, tryptophan, and D/ L-methionine are common feed additives. (Leuchtenberger, W. (1996) Amino aids – technical production and use, p. 466-502 in Rehm *et al.* (eds.) Biotechnology vol. 6, chapter 14a, VCH: Weinheim). Additionally, these amino acids have been found to be useful as precursors for the synthesis of synthetic amino acids and proteins, such as N-acetylcysteine, S-carboxymethyl-L-cysteine, (S)-5-hydroxytryptophan, and others described in Ulmann's Encyclopedia of Industrial Chemistry, vol. A2, p. 57-97, VCH: Weinheim, 1985.

The biosynthesis of these natural amino acids in organisms capable of 10 producing them, such as bacteria, has been well characterized (for review of bacterial amino acid biosynthesis and regulation thereof, see Umbarger, H.E.(1978) Ann. Rev. Biochem. 47: 533-606). Glutamate is synthesized by the reductive amination of α ketoglutarate, an intermediate in the citric acid cycle. Glutamine, proline, and arginine are each subsequently produced from glutamate. The biosynthesis of serine is a three-15 step process beginning with 3-phosphoglycerate (an intermediate in glycolysis), and resulting in this amino acid after oxidation, transamination, and hydrolysis steps. Both cysteine and glycine are produced from serine; the former by the condensation of homocysteine with serine, and the latter by the transferal of the side-chain β-carbon atom to tetrahydrofolate, in a reaction catalyzed by serine transhydroxymethylase. 20 Phenylalanine, and tyrosine are synthesized from the glycolytic and pentose phosphate pathway precursors erythrose 4-phosphate and phosphoenolpyruvate in a 9-step biosynthetic pathway that differ only at the final two steps after synthesis of prephenate. Tryptophan is also produced from these two initial molecules, but its synthesis is an 11step pathway. Tyrosine may also be synthesized from phenylalanine, in a reaction catalyzed by phenylalanine hydroxylase. Alanine, valine, and leucine are all biosynthetic products of pyruvate, the final product of glycolysis. Aspartate is formed from oxaloacetate, an intermediate of the citric acid cycle. Asparagine, methionine, threonine, and lysine are each produced by the conversion of aspartate. Isoleucine is formed from threonine. A complex 9-step pathway results in the production of histidine 30 from 5-phosphoribosyl-1-pyrophosphate, an activated sugar.

Amino acids in excess of the protein synthesis needs of the cell cannot be stored, and are instead degraded to provide intermediates for the major metabolic pathways of

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the cell (for review see Stryer, L. Biochemistry 3rd ed. Ch. 21 "Amino Acid Degradation and the Urea Cycle" p. 495-516 (1988)). Although the cell is able to convert unwanted amino acids into useful metabolic intermediates, amino acid production is costly in terms of energy, precursor molecules, and the enzymes necessary to synthesize them.

Thus it is not surprising that amino acid biosynthesis is regulated by feedback inhibition, in which the presence of a particular amino acid serves to slow or entirely stop its own production (for overview of feedback mechanisms in amino acid biosynthetic pathways, see Stryer, L. Biochemistry, 3rd ed. Ch. 24: "Biosynthesis of Amino Acids and Heme" p. 575-600 (1988)). Thus, the output of any particular amino acid is limited by the amount of that amino acid present in the cell.

B. Vitamin, Cofactor, and Nutraceutical Metabolism and Uses

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Vitamins, cofactors, and nutraceuticals comprise another group of molecules which the higher animals have lost the ability to synthesize and so must ingest, although they are readily synthesized by other organisms, such as bacteria. These molecules are either bioactive substances themselves, or are precursors of biologically active substances which may serve as electron carriers or intermediates in a variety of metabolic pathways. Aside from their nutritive value, these compounds also have significant industrial value as coloring agents, antioxidants, and catalysts or other processing aids. (For an overview of the structure, activity, and industrial applications of these compounds, see, for example, Ullman's Encyclopedia of Industrial Chemistry, "Vitamins" vol. A27, p. 443-613, VCH: Weinheim, 1996.) The term "vitamin" is artrecognized, and includes nutrients which are required by an organism for normal functioning, but which that organism cannot synthesize by itself. The group of vitamins may encompass cofactors and nutraceutical compounds. The language "cofactor" includes nonproteinaceous compounds required for a normal enzymatic activity to occur. Such compounds may be organic or inorganic; the cofactor molecules of the invention are preferably organic. The term "nutraceutical" includes dietary supplements having health benefits in plants and animals, particularly humans. Examples of such molecules are vitamins, antioxidants, and also certain lipids (e.g., polyunsaturated fatty acids).

The biosynthesis of these molecules in organisms capable of producing them, such as bacteria, has been largely characterized (Ullman's Encyclopedia of Industrial Chemistry, "Vitamins" vol. A27, p. 443-613, VCH: Weinheim, 1996; Michal, G. (1999) Biochemical Pathways: An Atlas of Biochemistry and Molecular Biology, John Wiley & Sons; Ong, A.S., Niki, E. & Packer, L. (1995) "Nutrition, Lipids, Health, and Disease" Proceedings of the UNESCO/Confederation of Scientific and Technological Associations in Malaysia, and the Society for Free Radical Research – Asia, held Sept. 1-3, 1994 at Penang, Malaysia, AOCS Press: Champaign, IL X, 374 S).

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Thiamin (vitamin B₁) is produced by the chemical coupling of pyrimidine and thiazole moieties. Riboflavin (vitamin B₂) is synthesized from guanosine-5'-triphosphate (GTP) and ribose-5'-phosphate. Riboflavin, in turn, is utilized for the synthesis of flavin mononucleotide (FMN) and flavin adenine dinucleotide (FAD). The family of compounds collectively termed 'vitamin B₆' (e.g., pyridoxine, pyridoxamine, pyridoxa-5'-phosphate, and the commercially used pyridoxin hydrochloride) are all derivatives of the common structural unit, 5-hydroxy-6-methylpyridine. Pantothenate (pantothenic acid. (R)-(+)-N-(2,4-dihydroxy-3,3-dimethyl-1-oxobutyl)-β-alanine) can be produced either by chemical synthesis or by fermentation. The final steps in pantothenate biosynthesis consist of the ATP-driven condensation of β-alanine and pantoic acid. The enzymes responsible for the biosynthesis steps for the conversion to pantoic acid, to βalanine and for the condensation to panthotenic acid are known. The metabolically active form of pantothenate is Coenzyme A, for which the biosynthesis proceeds in 5 enzymatic steps. Pantothenate, pyridoxal-5'-phosphate, cysteine and ATP are the precursors of Coenzyme A. These enzymes not only catalyze the formation of panthothante, but also the production of (R)-pantoic acid, (R)-pantolacton, (R)panthenol (provitamin B₅), pantetheine (and its derivatives) and coenzyme A.

Biotin biosynthesis from the precursor molecule pimeloyl-CoA in microorganisms has been studied in detail and several of the genes involved have been identified. Many of the corresponding proteins have been found to also be involved in Fe-cluster synthesis and are members of the nifS class of proteins. Lipoic acid is derived from octanoic acid, and serves as a coenzyme in energy metabolism, where it becomes part of the pyruvate dehydrogenase complex and the α -ketoglutarate dehydrogenase complex. The folates are a group of substances which are all derivatives

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of folic acid, which is turn is derived from L-glutamic acid, p-amino-benzoic acid and 6-methylpterin. The biosynthesis of folic acid and its derivatives, starting from the metabolism intermediates guanosine-5'-triphosphate (GTP), L-glutamic acid and p-amino-benzoic acid has been studied in detail in certain microorganisms.

Corrinoids (such as the cobalamines and particularly vitamin B₁₂) and porphyrines belong to a group of chemicals characterized by a tetrapyrole ring system. The biosynthesis of vitamin B₁₂ is sufficiently complex that it has not yet been completely characterized, but many of the enzymes and substrates involved are now known. Nicotinic acid (nicotinate), and nicotinamide are pyridine derivatives which are also termed 'niacin'. Niacin is the precursor of the important coenzymes NAD (nicotinamide adenine dinucleotide) and NADP (nicotinamide adenine dinucleotide phosphate) and their reduced forms.

The large-scale production of these compounds has largely relied on cell-free chemical syntheses, though some of these chemicals have also been produced by large-scale culture of microorganisms, such as riboflavin, Vitamin B₆, pantothenate, and biotin. Only Vitamin B₁₂ is produced solely by fermentation, due to the complexity of its synthesis. *In vitro* methodologies require significant inputs of materials and time, often at great cost.

20 C. Purine, Pyrimidine, Nucleoside and Nucleotide Metabolism and Uses

Purine and pyrimidine metabolism genes and their corresponding proteins are important targets for the therapy of tumor diseases and viral infections. The language "purine" or "pyrimidine" includes the nitrogenous bases which are constituents of nucleic acids, co-enzymes, and nucleotides. The term "nucleotide" includes the basic structural units of nucleic acid molecules, which are comprised of a nitrogenous base, a pentose sugar (in the case of RNA, the sugar is ribose; in the case of DNA, the sugar is D-deoxyribose), and phosphoric acid. The language "nucleoside" includes molecules which serve as precursors to nucleotides, but which are lacking the phosphoric acid moiety that nucleotides possess. By inhibiting the biosynthesis of these molecules, or their mobilization to form nucleic acid molecules, it is possible to inhibit RNA and DNA synthesis; by inhibiting this activity in a fashion targeted to cancerous cells, the ability of tumor cells to divide and replicate may be inhibited. Additionally, there are

nucleotides which do not form nucleic acid molecules, but rather serve as energy stores (i.e., AMP) or as coenzymes (i.e., FAD and NAD).

Several publications have described the use of these chemicals for these medical indications, by influencing purine and/or pyrimidine metabolism (e.g. Christopherson, R.I. and Lyons, S.D. (1990) "Potent inhibitors of de novo pyrimidine and purine biosynthesis as chemotherapeutic agents." Med. Res. Reviews 10: 505-548). Studies of enzymes involved in purine and pyrimidine metabolism have been focused on the development of new drugs which can be used, for example, as immunosuppressants or anti-proliferants (Smith, J.L., (1995) "Enzymes in nucleotide synthesis." Curr. Opin. Struct. Biol. 5: 752-757; (1995) Biochem Soc. Transact. 23: 877-902). However, purine and pyrimidine bases, nucleosides and nucleotides have other utilities: as intermediates in the biosynthesis of several fine chemicals (e.g., thiamine, S-adenosyl-methionine, folates, or riboflavin), as energy carriers for the cell (e.g., ATP or GTP), and for chemicals themselves, commonly used as flavor enhancers (e.g., IMP or GMP) or for several medicinal applications (see, for example, Kuninaka, A. (1996) Nucleotides and Related Compounds in Biotechnology vol. 6, Rehm et al., eds. VCH: Weinheim, p. 561-612). Also, enzymes involved in purine, pyrimidine, nucleoside, or nucleotide metabolism are increasingly serving as targets against which chemicals for crop protection, including fungicides, herbicides and insecticides, are developed.

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The metabolism of these compounds in bacteria has been characterized (for reviews see, for example, Zalkin, H. and Dixon, J.E. (1992) "de novo purine nucleotide biosynthesis", in: Progress in Nucleic Acid Research and Molecular Biology, vol. 42, Academic Press:, p. 259-287; and Michal, G. (1999) "Nucleotides and Nucleosides", Chapter 8 in: Biochemical Pathways: An Atlas of Biochemistry and Molecular Biology, Wiley: New York). Purine metabolism has been the subject of intensive research, and is essential to the normal functioning of the cell. Impaired purine metabolism in higher animals can cause severe disease, such as gout. Purine nucleotides are synthesized from ribose-5-phosphate, in a series of steps through the intermediate compound inosine-5'-phosphate (IMP), resulting in the production of guanosine-5'-monophosphate (GMP) or adenosine-5'-monophosphate (AMP), from which the triphosphate forms utilized as nucleotides are readily formed. These compounds are also utilized as energy stores, so their degradation provides energy for many different biochemical processes in the cell.

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Pyrimidine biosynthesis proceeds by the formation of uridine-5'-monophosphate (UMP) from ribose-5-phosphate. UMP, in turn, is converted to cytidine-5'-triphosphate (CTP). The deoxy- forms of all of these nucleotides are produced in a one step reduction reaction from the diphosphate ribose form of the nucleotide to the diphosphate deoxyribose form of the nucleotide. Upon phosphorylation, these molecules are able to participate in DNA synthesis.

D. Trehalose Metabolism and Uses

Trehalose consists of two glucose molecules, bound in α, α-1,1 linkage. It is commonly used in the food industry as a sweetener, an additive for dried or frozen foods, and in beverages. However, it also has applications in the pharmaceutical, cosmetics and biotechnology industries (see, for example, Nishimoto *et al.*, (1998) U.S. Patent No. 5,759,610; Singer, M.A. and Lindquist, S. (1998) *Trends Biotech.* 16: 460-467; Paiva, C.L.A. and Panek, A.D. (1996) *Biotech. Ann. Rev.* 2: 293-314; and Shiosaka, M. (1997) J. Japan 172: 97-102). Trehalose is produced by enzymes from many microorganisms and is naturally released into the surrounding medium, from which it can be collected using methods known in the art.

II. Resistance to Damage from Chemicals, Environmental Stress, and Antibiotics

Production of fine chemicals is typically performed by large-scale culture of bacteria developed to produce and secrete large quantities of these molecules. However, this type of large-scale fermentation results in the subjection of the microorganisms to stresses of various kinds. These stresses include environmental stress and chemical stress.

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A. Resistance to Environmental Stress

Examples of environmental stresses typically encountered in large-scale fermentative culture include mechanical stress, heat stress, stress due to limited oxygen, stress due to oxygen radicals, pH stress, and osmotic stress. The stirring mechanism used in most large-scale fermentors to ensure aeration of the culture produces heat, thus increasing the temperature of the culture. Increases in temperature induce the well-characterized heat shock response, in which a set of proteins are expressed which not

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only aid in the survival of the bacterium in the face of high temperatures, but also increase survival in response to a number of other environmental stresses (see Neidhardt, F.C., et al., eds. (1996) E. coli and Salmonella. ASM Press: Washington, D.C., p. 1382-1399; Wosten, M. M. (1998) FEMS Microbiology Reviews 22(3): 127-50; Bahl, H. et al. (1995) FEMS Microbiology Reviews 17(3): 341-348; Zimmerman, J.L., Cohill, P.R. (1991) New Biologist 3(7): 641-650; Samali, A., and Orrenius, S. (1998) Cell. Stress Chaperones 3(4): 228-236, and references contained therein from each of these citations). Regulation of the heat shock response in bacteria is facilitated by specific sigma factors and other cellular regulators of gene expression (Hecker, M., 10 Volker, U (1998). Molecular Microbiology 29(5): 1129-1136). One of the largest problems that the cell encounters when exposed to high temperature is that protein folding is impaired; nascent proteins have sufficient kinetic energy in high temperature circumstances that it is difficult for the growing polypeptide chain to remain in a stable conformation long enough to fold properly. Thus, two of the key types of proteins expressed during the heat shock response consist of chaperones (proteins which assist in the folding or unfolding of other proteins – see, e.g., Fink, A.L. (1999) Physiol. Rev. 79(2): 425-449), and proteases, which can destroy any improperly folded proteins. Examples of chaperones expressed during the heat shock response include GroEL and DNAK; proteases known to be expressed during this cellular reaction to heat shock 20 include Lon, FtsH, and ClpB.

Other environmental stresses besides heat may also provoke a stress response. Though the fermentor stirring process is meant to introduce oxygen into the culture, oxygen may remain in limited supply, particularly when the culture is advanced in growth and the oxygen needs of the culture are thereby increased; an insufficient supply of oxygen is another stress for the microorganism. Cells in fermentor cultures are also subjected to a number of osmotic stresses, particularly when nutrients are added to the culture, resulting in a high extracellular and low intracellular concentration of these molecules. Further, the large quantities of the desired molecules produced by these organisms in culture may contribute to osmotic stress of the bacteria. Lastly, aerobic metabolism such as that used by *C. glutamicum* results in carbon dioxide as a waste product; secretion of this molecule may acidify the culture medium due to conversion of this molecule to carboxylic acid. Thus, bacteria in culture are also frequently subjected

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to acidic pH stress. The converse may also be true – when high levels of basic waste molecules such as ammonium are present in the culture medium, the bacteria in culture may be subjected to basic pH stress as well.

To combat such environmental stresses, bacteria have elegant gene systems which are expressed upon exposure to one or more stresses, such as the aforementioned heat shock system. Genes expressed in response to osmotic stress, for example, encode proteins capable of transporting or synthesizing compatible solutes such that osmotic intake or export of a particular molecule is slowed to manageable levels. Other examples of stress-induced bacterial proteins are those involved in trehalose biosynthesis, those encoding enzymes involved in ppGpp metabolism, those involved in signal transduction, particularly those encoding two-component systems which are sensitive to osmotic pressure, and those encoding transcription factors which are responsive to a variety of stress factors (e.g., RssB analogues and/or sigma factors). Many other such genes and their protein products are known in the art.

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B. Resistance to Chemical Stress

Aside from environmental stresses, cells may also experience a number of chemical stresses. These may fall into two categories. The first are natural waster products of metabolism and other cellular processes which are secreted by the cell to the surrounding medium. The second are chemicals present in the extracellular medium which do not originate from the cell. Generally, when cells excrete toxic waste products from the concentrated intracellular cytoplasm into the relatively much more dilute extracellular medium, these products dissipate such that extracellular levels of the possibly toxic compound are quite low. However, in large-scale fermentative culture of the bacterium, this may not be the case: so many bacteria are grown in a relatively small environment and at such a high metabolic rate that waste products may accumulate in the medium to nearly toxic levels. Examples of such wastes are carbon dioxide, metal ions, and reactive oxygen species such as hydrogen peroxide. These compounds may interfere with the activity or structure of cell surface molecules, or may re-enter the cell, where they can seriously damage proteins and nucleic acids alike. Certain other chemicals hazardous to the normal functioning of cells may be naturally found in the extracellular medium. For example, metal ions such as mercury, cadmium, nickel or

copper are frequently found in water sources, and may form tight complexes with cellular enzymes which prevent the normal functioning of these proteins.

C. Resistance to Antibiotics

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Bacteriocidal proteins or antibiotics, may also be found in the extracellular milieu, either through the intervention of the researcher, or as a natural product from another organism, utilized to gain a competitive advantage. Microorganisms have several art-known mechanisms to protect themselves against antimicrobial chemicals. Degradation, modification, and export of compounds toxic to the cell are common methods by which microorganisms eliminate or detoxify antibiotics. Cytoplasmic 'efflux-pumps' are known in several prokaryotes and show similarities to the so-called 'multidrug resistance' proteins from higher eukaryotes (Neyfakh, A. A., et al. (1991) Proc. Natl. Acad. Sci. USA 88: 4781-4785). Examples of such proteins include emrAB from E. coli (Lomovskaya, O. and K. Lewis (1992) Proc. Natl. Acad. Sci. USA 89: 8938-8942), lmrB from B. subtilis (Kumano, M. et al. (1997) Microbiology 143: 2775-2782), smr from S. aureus (Grinius, L.G. et al. (1992) Plasmid 27: 119-129) or cmr from C. glutamicum (Kaidoh, K. et al. (1997) Micro. Drug Resist. 3: 345-350). .C. glutamicum itself is non-pathogenic, in contrast to several other members of the genus Corynebacterium, such as C. diphtheriae or C. pseudotuberculosis. Several pathogenic Corynebacteria are known to have multiple resistances against a variety of antibiotics, such as C. jeikeium and C. urealyticum (Soriano, F. et al. (1995) Antimicrob. Agents Chemother. 39: 208-214).

Lincosamides are recognized as effective antibiotics against Corynebacterium species (Soriano, F. et al. (1995) Antimicrob. Agents Chemother. 39: 208-214). An unexpected result of the present invention was the identification of a gene encoding a lincosamide-resistance protein (in particular, a lincomycin-resistance protein). The LMRB protein from C. glutamicum shows 40% homology to the product of the lmrB gene from B. subtilis (see Genbank accession no. AL009126), as calculated using version 1.7 of the program CLUSTALW (Thompson, J.D., Higgins, D.G., Gibson, T. J. (1994) Nucl. Acids Res. 22: 4673-4680) using standard parameters (PAIRWISE ALIGNMENT PARAMETERS: slow/accurate alignments: Gap Open Penalty = 10.00, Gap Extension Penalty = 0.10, Protein weight matrix = BLOSUM 30, DNA weight

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matrix = IUB, Fast/Approximate alignments: Gap penalty = 3, K-tuple (word) size = 1, No. of top diagonals = 5, Window size = 5, Toggle Slow/Fast pairwise alignments = slow. Multiple alignment parameters: Gap Opening Penalty = 10.00, Gap Extension Penalty = 0.05, Delay divergent sequences = 40%, DNA transitions weight = 0.50, Protein weight matrix = BLOSUM series, DNA weight matrix = IUB, Use negative matrix = OFF).

Environmental stress, chemical stress, and antibiotic or other antimicrobial stress may influence the behavior of the microorganisms during fermentor culture, and may have an impact on the production of the desired compound from these organisms. 10 For example, osmotic stress of a microorganism may cause inappropriate or inappropriately rapid uptake of one or more compounds which can ultimately lead to cellular damage or death due to osmotic shock. Similarly, chemicals present in the culture, either exogenously added (e.g., antimicrobial compounds intended to eliminate unwanted microbes) or generated by the bacteria themselves (e.g., waste compounds such as heavy metals or oxygen radicals, or even antimicrobial compounds) may result in inhibition of fine chemical production or even death of the organism. The genes of the invention encode C. glutamicum proteins which act to prevent cell damage or death, by specifically counteracting the source or effect of the environmental or chemical stress.

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III. Elements and Methods of the Invention

The present invention is based, at least in part, on the discovery of novel molecules, referred to herein as SRT nucleic acid and protein molecules, which increase the ability of C. glutamicum to survive in chemically or environmentally hazardous settings. In one embodiment, the SRT molecules function to confer resistance to one or more environmental or chemical stresses to C. glutamicum. In a preferred embodiment, the activity of the SRT molecules of the present invention has an impact on the production of a desired fine chemical by this organism. In a particularly preferred embodiment, the SRT molecules of the invention are modulated in activity, such that the yield, production, and/or efficiency of production of one or more fine chemicals from C. glutamicum is also modulated.

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The language, "SRT protein" or "SRT polypeptide" includes proteins which participate in the resistance of C. glutamicum to one or more environmental or chemical stresses. Examples of SRT proteins include those encoded by the SRT genes set forth in Table 1 and by the odd-numbered SEQ ID NOs. The terms "SRT gene" or "SRT nucleic acid sequence" include nucleic acid sequences encoding an SRT protein, which consist of a coding region and also corresponding untranslated 5' and 3' sequence regions. Examples of SRT genes include those set forth in Table 1. The terms "production" or "productivity" are art-recognized and include the concentration of the fermentation product (for example, the desired fine chemical) formed within a given time and a given fermentation volume (e.g., kg product per hour per liter). The term "efficiency of production" includes the time required for a particular level of production to be achieved (for example, how long it takes for the cell to attain a particular rate of output of a fine chemical). The term "yield" or "product/carbon yield" is art-recognized and includes the efficiency of the conversion of the carbon source into the product (i.e., fine chemical). This is generally written as, for example, kg product per kg carbon source. By increasing the yield or production of the compound, the quantity of recovered molecules, or of useful recovered molecules of that compound in a given amount of culture over a given amount of time is increased. The terms "biosynthesis" or a "biosynthetic pathway" are art-recognized and include the synthesis of a compound, preferably an organic compound, by a cell from intermediate compounds in what may be a multistep and highly regulated process. The terms "degradation" or a "degradation pathway" are art-recognized and include the breakdown of a compound, preferably an organic compound, by a cell to degradation products (generally speaking, smaller or less complex molecules) in what may be a multistep and highly regulated process. The language "metabolism" is art-recognized and includes the totality of the biochemical reactions that take place in an organism. The metabolism of a particular compound, then, (e.g., the metabolism of an amino acid such as glycine) comprises the overall biosynthetic, modification, and degradation pathways in the cell related to this compound. The terms "resistance" and "tolerance" are art-known and include the ability of a cell to not be affected by exposure to a chemical or an environment which would otherwise be detrimental to the normal functioning of these organisms. The terms "stress" or "hazard" include factors which are detrimental to the normal functioning of

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cells such as *C. glutamicum*. Examples of stresses include "chemical stress", in which a cell is exposed to one or more chemicals which are detrimental to the cell, and "environmental stress" where a cell is exposed to an environmental condition outside of those to which it is adapted. Chemical stresses may be either natural metabolic waste products such as, but not limited to reactive oxygen species or carbon dioxide, or chemicals otherwise present in the environment, including, but not limited to heavy metal ions or bacteriocidal proteins such as antibiotics. Environmental stresses may be, but are not limited to temperatures outside of the normal range, suboptimal oxygen availability, osmotic pressures, or extremes of pH, for example.

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In another embodiment, the SRT molecules of the invention are capable of modulating the production of a desired molecule, such as a fine chemical, in a microorganism such as C. glutamicum. Using recombinant genetic techniques, one or more of the SRT proteins of the invention may be manipulated such that its function is modulated. The alteration of activity of stress response, resistance or tolerance genes such that the cell is increased in tolerance to one or more stresses may improve the ability of that cell to grow and multiply in the relatively stressful conditions of largescale fermentor culture. For example, by overexpressing or engineering a heat-shock induced chaperone molecule such that it is optimized in activity, one may increase the ability of the bacterium to correctly fold proteins in the face of nonoptimal temperature conditions. By having fewer misfolded (and possibly misregulated or nonfunctional) proteins, the cell is increased in its ability to function normally in such a culture, which should in turn provide increased viability. This overall increase in number of cells having greater viability and activity in the culture should also result in an increase in the yield, production, and/or efficiency of production of one or more desired fine chemicals, due at least to the relatively greater number of cells producing these chemicals in the culture.

The isolated nucleic acid sequences of the invention are contained within the genome of a *Corynebacterium glutamicum* strain available through the American Type Culture Collection, given designation ATCC 13032. The nucleotide sequence of the isolated *C. glutamicum* SRT DNAs and the predicted amino acid sequences of the *C. glutamicum* SRT proteins are shown the Sequence Listing as odd-numbered SEQ ID NOs and even-numbered SEQ ID NOs, respectively...

Computational analyses were performed which classified and/or identified these nucleotide sequences as sequences which encode chemical and environmental stress, resistance, and tolerance proteins.

The present invention also pertains to proteins which have an amino acid sequence which is substantially homologous to an amino acid sequence of the invention (e.g., the sequence of an even-numbered SEQ ID NO of the Sequence Listing). As used herein, a protein which has an amino acid sequence which is substantially homologous to a selected amino acid sequence is least about 50% homologous to the selected amino acid sequence, e.g., the entire selected amino acid sequence. A protein which has an amino acid sequence which is substantially homologous to a selected amino acid sequence can also be least about 50-60%, preferably at least about 60-70%, and more preferably at least about 70-80%, 80-90%, or 90-95%, and most preferably at least about 96%, 97%, 98%, 99% or more homologous to the selected amino acid sequence. Ranges and identity values intermediate to the above-recited values, (e.g., 75%-80% identical, 85-87% identical, 91-92% identical) are also intended to be encompassed by the present invention. For example, ranges of identity values using a combination of any of the above values recited as upper and/or lower limits are intended to be included.

The SRT proteins or biologically active portions or fragments thereof of the invention can confer resistance or tolerance to one or more chemical or environmental stresses, or may have one or more of the activities set forth in Table 1.

Various aspects of the invention are described in further detail in the following subsections:

A. Isolated Nucleic Acid Molecules

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One aspect of the invention pertains to isolated nucleic acid molecules that encode SRT polypeptides or biologically active portions thereof, as well as nucleic acid fragments sufficient for use as hybridization probes or primers for the identification or amplification of SRT-encoding nucleic acid (e.g., SRT DNA). As used herein, the term "nucleic acid molecule" is intended to include DNA molecules (e.g., cDNA or genomic DNA) and RNA molecules (e.g., mRNA) and analogs of the DNA or RNA generated using nucleotide analogs. This term also encompasses untranslated sequence located at both the 3' and 5' ends of the coding region of the gene: at least about 100 nucleotides

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of sequence upstream from the 5' end of the coding region and at least about 20 nucleotides of sequence downstream from the 3'end of the coding region of the gene. The nucleic acid molecule can be single-stranded or double-stranded, but preferably is double-stranded DNA. An "isolated" nucleic acid molecule is one which is separated from other nucleic acid molecules which are present in the natural source of the nucleic acid. Preferably, an "isolated" nucleic acid is free of sequences which naturally flank the nucleic acid (*i.e.*, sequences located at the 5' and 3' ends of the nucleic acid) in the genomic DNA of the organism from which the nucleic acid is derived. For example, in various embodiments, the isolated SRT nucleic acid molecule can contain less than about 5 kb, 4kb, 3kb, 2kb, 1 kb, 0.5 kb or 0.1 kb of nucleotide sequences which naturally flank the nucleic acid molecule in genomic DNA of the cell from which the nucleic acid is derived (*e.g.*, a *C. glutamicum* cell). Moreover, an "isolated" nucleic acid molecule, such as a DNA molecule, can be substantially free of other cellular material, or culture medium when produced by recombinant techniques, or chemical precursors or other chemicals when chemically synthesized.

A nucleic acid molecule of the present invention, e.g., a nucleic acid molecule

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having a nucleotide sequence of an odd-numbered SEQ ID NO of the Sequence Listing, or a portion thereof, can be isolated using standard molecular biology techniques and the sequence information provided herein. For example, a C. glutamicum SRT DNA can be isolated from a C. glutamicum library using all or portion of one of the odd-numbered SEQ ID NO sequences of the Sequence Listing as a hybridization probe and standard hybridization techniques (e.g., as described in Sambrook, J., Fritsh, E. F., and Maniatis, T. Molecular Cloning: A Laboratory Manual. 2nd, ed., Cold Spring Harbor Laboratory, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, 1989). Moreover, a nucleic acid molecule encompassing all or a portion of one of the nucleic acid sequences of the invention (e.g., an odd-numbered SEQ ID NO:) can be isolated by the polymerase chain reaction using oligonucleotide primers designed based upon this sequence (e.g., a nucleic acid molecule encompassing all or a portion of one of the nucleic acid sequences of the invention (e.g., an odd-numbered SEQ ID NO of the Sequence Listing) can be isolated by the polymerase chain reaction using 30 oligonucleotide primers designed based upon this same sequence). For example, mRNA can be isolated from normal endothelial cells (e.g., by the guanidinium-thiocyanate

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extraction procedure of Chirgwin et al. (1979) Biochemistry 18: 5294-5299) and DNA can be prepared using reverse transcriptase (e.g., Moloney MLV reverse transcriptase, available from Gibco/BRL, Bethesda, MD; or AMV reverse transcriptase, available from Seikagaku America, Inc., St. Petersburg, FL). Synthetic oligonucleotide primers for polymerase chain reaction amplification can be designed based upon one of the nucleotide sequences shown in the Sequence Listing. A nucleic acid of the invention can be amplified using cDNA or, alternatively, genomic DNA, as a template and appropriate oligonucleotide primers according to standard PCR amplification techniques. The nucleic acid so amplified can be cloned into an appropriate vector and characterized by DNA sequence analysis. Furthermore, oligonucleotides corresponding to an SRT nucleotide sequence can be prepared by standard synthetic techniques, e.g., using an automated DNA synthesizer.

In a preferred embodiment, an isolated nucleic acid molecule of the invention comprises one of the nucleotide sequences shown in the Sequence Listing. The nucleic 15 acid sequences of the invention, as set forth in the Sequence Listing, correspond to the Corynebacterium glutamicum SRT DNAs of the invention. This DNA comprises sequences encoding SRT proteins (i.e., the "coding region", indicated in each oddnumbered SEQ ID NO: sequence in the Sequence Listing), as well as 5' untranslated sequences and 3' untranslated sequences, also indicated in each odd-numbered SEO ID NO: in the Sequence Listing. Alternatively, the nucleic acid molecule can comprise only the coding region of any of the nucleic acid sequences of the Sequence Listing.

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For the purposes of this application, it will be understood that each of the nucleic acid and amino acid sequences set forth in the Sequence Listing has an identifying RXA, RXN, or RXS number having the designation "RXA", "RXN", or "RXS" followed by 5 digits (i.e., RXA01524, RXN00493, or RXS01027). Each of the nucleic acid sequences comprises up to three parts: a 5' upstream region, a coding region, and a downstream region. Each of these three regions is identified by the same RXA, RXN, or RXS designation to eliminate confusion. The recitation "one of the odd-numbered sequences of the Sequence Listing", then, refers to any of the nucleic acid sequences in the Sequence Listing, , which may be also be distinguished by their differing RXA, RXN, or RXS designations. The coding region of each of these sequences is translated into a corresponding amino acid sequence, which is also et forth in the Sequence Listing, as an

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even-numbered SEQ ID NO: immediately following the corresponding nucleic acid sequence. For example, the coding region for RXA01524 is set forth in SEQ ID NO:1, while the amino acid sequence which it encodes is set forth as SEQ ID NO:2. The sequences of the nucleic acid molecules of the invention are identified by the same

5 RXA, RXN, or RXS designations as the amino acid molecules which they encode, such that they can be readily correlated. For example, the amino acid sequence designated RXA01524 is a translation of the coding region of the nucleotide sequence of nucleic acid molecule RXA01524, the amino acid sequence designated RXN00034 is a translation of the coding region of the nucleotide sequence of nucleic acid molecule

10 RXN00034, and the amino acid sequence in designated RXS00568 is a translation of the coding region of the nucleotide sequence of nucleic acid molecule RXS00568. The correspondence between the RXA, RXN, and RXS nucleotide and amino acid sequences of the invention and their assigned SEQ ID NOs is set forth in Table 1.

Several of the genes of the invention are "F-designated genes". An F-designated gene includes those genes set forth in Table 1 which have an 'F' in front of the RXA, RXN, or RXS designation. For example, SEQ ID NO:7, designated, as indicated on Table 1, as "F RXA00498", is an F-designated gene, as are SEQ ID NOs: 25, 33, and 37 (designated on Table 1 as "F RXA01345", "F RXA02543", and "F RXA02282", respectively).

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In one embodiment, the nucleic acid molecules of the present invention are not intended to include those compiled in Table 2. In the case of the dapD gene, a sequence for this gene was published in Wehrmann, A., et al. (1998) J. Bacteriol. 180(12): 3159-3165. However, the sequence obtained by the inventors of the present application is significantly longer than the published version. It is believed that the published version relied on an incorrect start codon, and thus represents only a fragment of the actual coding region.

In another preferred embodiment, an isolated nucleic acid molecule of the invention comprises a nucleic acid molecule which is a complement of one of the nucleotide sequences of the invention (e.g., a sequence of an odd-numbered SEQ ID NO: of the Sequence Listing, or a portion thereof. A nucleic acid molecule which is complementary to one of the nucleotide sequences of the invention is one which is sufficiently complementary to one of the nucleotide sequences shown in the Sequence

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Listing (e.g., the sequence of an odd-numbered SEQ ID NO:) such that it can hybridize to one of the nucleotide sequences of the invention, thereby forming a stable duplex.

In still another preferred embodiment, an isolated nucleic acid molecule of the invention comprises a nucleotide sequence which is at least about 50%, 51%, 52%, 53%, 54%, 55%, 56%, 57%, 58%, 59%, or 60%, preferably at least about 61%, 62%, 63%, 64%, 65%, 66%, 67%, 68%, 69%, or 70%%, more preferably at least about 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, or 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, or 90%, or 91%, 92%, 93%, 94%, and even more preferably at least about 95%, 96%, 97%, 98%, 99% or more homologous to a nucleotide sequence of the invention (e.g., a sequence of an odd-numbered SEQ ID NO: of the Sequence Listing), or a portion thereof. Ranges and identity values intermediate to the above-recited ranges, (e.g., 70-90% identical or 80-95% identical) are also intended to be encompassed by the present invention. For example, ranges of identity values using a combination of any of the above values recited as upper and/or lower limits are intended to be included. In an additional preferred embodiment, an isolated nucleic acid molecule of the invention comprises a nucleotide sequence which hybridizes, e.g., hybridizes under stringent conditions, to one of the nucleotide sequences of the invention,, or a portion thereof.

Moreover, the nucleic acid molecule of the invention can comprise only a portion of the coding region of the sequence of one of the odd-numbered SEQ ID NOs of the Sequence Listing for example a fragment which can be used as a probe or primer or a fragment encoding a biologically active portion of an SRT protein. The nucleotide sequences determined from the cloning of the SRT genes from *C. glutamicum* allows for the generation of probes and primers designed for use in identifying and/or cloning SRT homologues in other cell types and organisms, as well as SRT homologues from other *Corynebacteria* or related species. The probe/primer typically comprises substantially purified oligonucleotide. The oligonucleotide typically comprises a region of nucleotide sequence that hybridizes under stringent conditions to at least about 12, preferably about 25, more preferably about 40, 50 or 75 consecutive nucleotides of a sense strand of one of the nucleotide sequences of the invention (*e.g.*, a sequence of one of the odd-numbered SEQ ID NOs of the Sequence Listing),, an anti-sense sequence of one of these sequences, or naturally occurring mutants thereof. Primers based on a nucleotide sequence of the invention can be used in PCR reactions to clone SRT homologues.

Probes based on the SRT nucleotide sequences can be used to detect transcripts or genomic sequences encoding the same or homologous proteins. In preferred embodiments, the probe further comprises a label group attached thereto, e.g. the label group can be a radioisotope, a fluorescent compound, an enzyme, or an enzyme cofactor. Such probes can be used as a part of a diagnostic test kit for identifying cells which misexpress an SRT protein, such as by measuring a level of an SRT-encoding nucleic acid in a sample of cells, e.g., detecting SRT mRNA levels or determining whether a genomic SRT gene has been mutated or deleted.

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In one embodiment, the nucleic acid molecule of the invention encodes a protein or portion thereof which includes an amino acid sequence which is sufficiently homologous to an amino acid sequence of the invention (e.g., a sequence of an evennumbered SEQ ID NO of the Sequence Listing) such that the protein or portion thereof maintains the ability to confer resistance or tolerance of C. glutamicum to one or more chemical or environmental stresses. As used herein, the language "sufficiently homologous" refers to proteins or portions thereof which have amino acid sequences which include a minimum number of identical or equivalent (e.g., an amino acid residue which has a similar side chain as an amino acid residue in a sequence of one of the evennumbered SEQ ID NOs of the Sequence Listing) amino acid residues to an amino acid sequence of the invention such that the protein or portion thereof is capable of participating in the resistance of C. glutamicum to one or more chemical or environmental stresses. Protein members of such metabolic pathways, as described herein, function to increase the resistance or tolerance of C. glutamicum to one or more environmental or chemical hazards or stresses. Examples of such activities are also described herein. Thus, "the function of an SRT protein" contributes to the overall resistance of C. glutamicum to elements of its surroundings which may impede its normal growth or functioning, and/or contributes, either directly or indirectly, to the yield, production, and/or efficiency of production of one or more fine chemicals. Examples of SRT protein activities are set forth in Table 1.

In another embodiment, the protein is at least about 50-60%, preferably at least about 60-70%, and more preferably at least about 70-80%, 80-90%, 90-95%, and most preferably at least about 96%, 97%, 98%, 99% or more homologous to an entire amino acid sequence of the invention (e.g., a sequence of an even-numbered SEQ ID NO: of

the Sequence Listing). Ranges and identity values intermediate to the above-recited values, (e.g., 75%-80% identical, 85-87% identical, or 91-92% identical) are also intended to be encompassed by the present invention. For example, ranges of identity values using a combination of any of the above values recited as upper and/or lower limits are intended to be included.

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Portions of proteins encoded by the SRT nucleic acid molecules of the invention are preferably biologically active portions of one of the SRT proteins. As used herein, the term "biologically active portion of an SRT protein" is intended to include a portion, e.g., a domain/motif, of an SRT protein that is capable of imparting resistance or tolerance to one or more environmental or chemical stresses or hazards, or has an activity as set forth in Table 1. To determine whether an SRT protein or a biologically active portion thereof can increase the resistance or tolerance of C. glutamicum to one or more chemical or environmental stresses or hazards, an assay of enzymatic activity may be performed. Such assay methods are well known to those of ordinary skill in the art, as detailed in Example 8 of the Exemplification.

Additional nucleic acid fragments encoding biologically active portions of an SRT protein can be prepared by isolating a portion of one of the amino acid sequences of the invention (e.g., a sequence of an even-numbered SEQ ID NO: of the Sequence Listing), expressing the encoded portion of the SRT protein or peptide (e.g., by recombinant expression *in vitro*) and assessing the activity of the encoded portion of the SRT protein or peptide.

The invention further encompasses nucleic acid molecules that differ from one of the nucleotide sequences of the invention (e.g., a sequence of an odd-numbered SEQ ID NO: of the Sequence Listing) (and portions thereof) due to degeneracy of the genetic code and thus encode the same SRT protein as that encoded by the nucleotide sequences of the invention. In another embodiment, an isolated nucleic acid molecule of the invention has a nucleotide sequence encoding a protein having an amino acid sequence shown in the Sequence Listing (e.g., an even-numbered SEQ ID NO:).. In a still further embodiment, the nucleic acid molecule of the invention encodes a full length C. glutamicum protein which is substantially homologous to an amino acid sequence of the invention (encoded by an open reading frame shown in an odd-numbered SEQ ID NO: of the Sequence Listing).

It will be understood by one of ordinary skill in the art that in one embodiment the sequences of the invention are not meant to include the sequences of the prior art, such as those Genbank sequences set forth in Tables 2 or 4 which were available prior to the present invention. In one embodiment, the invention includes nucleotide and amino acid sequences having a percent identity to a nucleotide or amino acid sequence of the invention which is greater than that of a sequence of the prior art (e.g., a Genbank sequence (or the protein encoded by such a sequence) set forth in Tables 2 or 4). For example, the invention includes a nucleotide sequence which is greater than and/or at least 39% identical to the nucleotide sequence designated RXA00084 (SEO ID NO:189), a nucleotide sequence which is greater than and/or at least 56% identical to the 10 nucleotide sequence designated RXA00605 (SEQ ID NO:11), and a nucleotide sequence which is greater than and/or at least 50% identical to the nucleotide sequence designated RXA00886 (SEQ ID NO:39). One of ordinary skill in the art would be able to calculate the lower threshold of percent identity for any given sequence of the invention by examining the GAP-calculated percent identity scores set forth in Table 4 for each of the three top hits for the given sequence, and by subtracting the highest GAP-calculated percent identity from 100 percent. One of ordinary skill in the art will also appreciate that nucleic acid and amino acid sequences having percent identities greater than the lower threshold so calculated (e.g., at least 50%, 51%, 52%, 53%, 54%, 55%, 56%, 57%, 58%, 59%, or 60%, preferably at least about 61%, 62%, 63%, 64%, 65%, 66%, 67%, 68%, 69%, or 70%, more preferably at least about 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, or 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, or 90%, or 91%, 92%, 93%, 94%, and even more preferably at least about 95%, 96%, 97%, 98%, 99% or more identical) are also encompassed by the invention.

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In addition to the C. glutamicum SRT nucleotide sequences set forth in the Sequence Listing as odd-numbered SEQ ID NOs, it will be appreciated by one of ordinary skill in the art that DNA sequence polymorphisms that lead to changes in the amino acid sequences of SRT proteins may exist within a population (e.g., the C. glutamicum population). Such genetic polymorphism in the SRT gene may exist among individuals within a population due to natural variation. As used herein, the terms "gene" and "recombinant gene" refer to nucleic acid molecules comprising an open reading frame encoding an SRT protein, preferably a C. glutamicum SRT protein. Such

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natural variations can typically result in 1-5% variance in the nucleotide sequence of the SRT gene. Any and all such nucleotide variations and resulting amino acid polymorphisms in SRT that are the result of natural variation and that do not alter the functional activity of SRT proteins are intended to be within the scope of the invention.

Nucleic acid molecules corresponding to natural variants and non-C. glutamicum homologues of the C. glutamicum SRT DNA of the invention can be isolated based on their homology to the C. glutamicum SRT nucleic acid disclosed herein using the C. glutamicum DNA, or a portion thereof, as a hybridization probe according to standard hybridization techniques under stringent hybridization conditions. Accordingly, in another embodiment, an isolated nucleic acid molecule of the invention is at least 15 nucleotides in length and hybridizes under stringent conditions to the nucleic acid molecule comprising a nucleotide sequence of an odd-numbered SEQ ID NO: of the Sequence Listing. In other embodiments, the nucleic acid is at least 30, 50, 100, 250 or more nucleotides in length. As used herein, the term "hybridizes under stringent conditions" is intended to describe conditions for hybridization and washing under which nucleotide sequences at least 60% homologous to each other typically remain hybridized to each other. Preferably, the conditions are such that sequences at least about 65%, more preferably at least about 70%, and even more preferably at least about 75% or more homologous to each other typically remain hybridized to each other. Such stringent conditions are known to those of ordinary skill in the art in the art and can be found in Ausubel et al., Current Protocols in Molecular Biology, John Wiley & Sons, N.Y. (1989), 6.3.1-6.3.6. A preferred, non-limiting example of stringent hybridization conditions are hybridization in 6X sodium chloride/sodium citrate (SSC) at about 45°C, followed by one or more washes in 0.2 X SSC, 0.1% SDS at 50-65°C. Preferably, an isolated nucleic acid molecule of the invention that hybridizes under stringent conditions to a nucleotide sequence of the invention corresponds to a naturally-occurring nucleic acid molecule. As used herein, a "naturally-occurring" nucleic acid molecule refers to an RNA or DNA molecule having a nucleotide sequence that occurs in nature (e.g., encodes a natural protein). In one embodiment, the nucleic acid encodes a natural C. glutamicum SRT protein.

In addition to naturally-occurring variants of the SRT sequence that may exist in the population, one of ordinary skill in the art will further appreciate that changes can be

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introduced by mutation into a nucleotide sequence of the invention, thereby leading to changes in the amino acid sequence of the encoded SRT protein, without altering the functional ability of the SRT protein. For example, nucleotide substitutions leading to amino acid substitutions at "non-essential" amino acid residues can be made in a nucleotide sequence of the invention. A "non-essential" amino acid residue is a residue that can be altered from the wild-type sequence of one of the SRT proteins (e.g., an even-numbered SEQ ID NO: of the Sequence Listing) without altering the activity of said SRT protein, whereas an "essential" amino acid residue is required for SRT protein activity. Other amino acid residues, however, (e.g., those that are not conserved or only semi-conserved in the domain having SRT activity) may not be essential for activity and thus are likely to be amenable to alteration without altering SRT activity.

Accordingly, another aspect of the invention pertains to nucleic acid molecules encoding SRT proteins that contain changes in amino acid residues that are not essential for SRT activity. Such SRT proteins differ in amino acid sequence from a sequence of an even-numbered SEQ ID NO: of the Sequence Listing yet retain at least one of the SRT activities described herein. In one embodiment, the isolated nucleic acid molecule comprises a nucleotide sequence encoding a protein, wherein the protein comprises an amino acid sequence at least about 50% homologous to an amino acid sequence of the invention and is capable of increasing the resistance or tolerance of C. glutamicum to one or more environmental or chemical stresses, or has one or more of the activities set forth in Table 1. Preferably, the protein encoded by the nucleic acid molecule is at least about 50-60% homologous to the amino acid sequence of one of the odd-numbered SEQ ID NOs of the Sequence Listing, more preferably at least about 60-70% homologous to one of these sequences, even more preferably at least about 70-80%, 80-90%, 90-95% homologous to one of these sequences in, and most preferably at least about 96%, 97%, 98%, or 99% homologous to one of the amino acid sequences of the invention.

To determine the percent homology of two amino acid sequences (e.g., one of the amino acid sequences of the invention and a mutant form thereof) or of two nucleic acids, the sequences are aligned for optimal comparison purposes (e.g., gaps can be introduced in the sequence of one protein or nucleic acid for optimal alignment with the other protein or nucleic acid). The amino acid residues or nucleotides at corresponding amino acid positions or nucleotide positions are then compared. When a position in one

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sequence (e.g., one of the amino acid sequences of the invention) is occupied by the same amino acid residue or nucleotide as the corresponding position in the other sequence (e.g., a mutant form of the amino acid sequence), then the molecules are homologous at that position (i.e., as used herein amino acid or nucleic acid "homology" is equivalent to amino acid or nucleic acid "identity"). The percent homology between the two sequences is a function of the number of identical positions shared by the sequences (i.e., % homology = # of identical positions/total # of positions x 100).

An isolated nucleic acid molecule encoding an SRT protein homologous to a protein sequence of the invention (e.g., a sequence of an even-numbered SEQ ID NO: of the Sequence Listing)can be created by introducing one or more nucleotide substitutions, additions or deletions into a nucleotide sequence of the invention such that one or more amino acid substitutions, additions or deletions are introduced into the encoded protein. Mutations can be introduced into one of the nucleotide sequences of the invention by standard techniques, such as site-directed mutagenesis and PCRmediated mutagenesis. Preferably, conservative amino acid substitutions are made at one or more predicted non-essential amino acid residues. A "conservative amino acid substitution" is one in which the amino acid residue is replaced with an amino acid residue having a similar side chain. Families of amino acid residues having similar side chains have been defined in the art. These families include amino acids with basic side chains (e.g., lysine, arginine, histidine), acidic side chains (e.g., aspartic acid, glutamic acid), uncharged polar side chains (e.g., glycine, asparagine, glutamine, serine, threonine, tyrosine, cysteine), nonpolar side chains (e.g., alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine, tryptophan), beta-branched side chains (e.g., threonine, valine, isoleucine) and aromatic side chains (e.g., tyrosine, phenylalanine, tryptophan, histidine). Thus, a predicted nonessential amino acid residue in an SRT protein is preferably replaced with another amino acid residue from the same side chain family. Alternatively, in another embodiment, mutations can be introduced randomly along all or part of an SRT coding sequence, such as by saturation mutagenesis, and the resultant mutants can be screened for an SRT activity described herein to identify mutants that retain SRT activity. Following mutagenesis of one the nucleotide sequence of one of the odd-numbered SEQ ID NOs of the Sequence Listing, the encoded protein can be expressed recombinantly and the activity of the protein can

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be determined using, for example, assays described herein (see Example 8 of the Exemplification).

In addition to the nucleic acid molecules encoding SRT proteins described above, another aspect of the invention pertains to isolated nucleic acid molecules which are antisense thereto. An "antisense" nucleic acid comprises a nucleotide sequence which is complementary to a "sense" nucleic acid encoding a protein, e.g., complementary to the coding strand of a double-stranded DNA molecule or complementary to an mRNA sequence. Accordingly, an antisense nucleic acid can hydrogen bond to a sense nucleic acid. The antisense nucleic acid can be complementary to an entire SRT coding strand, or to only a portion thereof. In one embodiment, an antisense nucleic acid molecule is antisense to a "coding region" of the coding strand of a nucleotide sequence encoding an SRT protein. The term "coding region" refers to the region of the nucleotide sequence comprising codons which are translated into amino acid residues (e.g., the entire coding region of SEQ ID NO.: 120 (RXA00600) comprises nucleotides 1 to 1098). In another embodiment, the antisense nucleic acid molecule is antisense to a "noncoding region" of the coding strand of a nucleotide sequence encoding SRT. The term "noncoding region" refers to 5' and 3' sequences which flank the coding region that are not translated into amino acids (i.e., also referred to as 5' and 3' untranslated regions).

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Given the coding strand sequences encoding SRT disclosed herein (e.g., the sequences set forth as odd-numbered SEQ ID NOs in the Sequence Listing), antisense nucleic acids of the invention can be designed according to the rules of Watson and Crick base pairing. The antisense nucleic acid molecule can be complementary to the entire coding region of SRT mRNA, but more preferably is an oligonucleotide which is antisense to only a portion of the coding or noncoding region of SRT mRNA. For example, the antisense oligonucleotide can be complementary to the region surrounding the translation start site of SRT mRNA. An antisense oligonucleotide can be, for example, about 5, 10, 15, 20, 25, 30, 35, 40, 45 or 50 nucleotides in length. An antisense nucleic acid of the invention can be constructed using chemical synthesis and enzymatic ligation reactions using procedures known in the art. For example, an antisense nucleic acid (e.g., an antisense oligonucleotide) can be chemically synthesized using naturally occurring nucleotides or variously modified nucleotides designed to

increase the biological stability of the molecules or to increase the physical stability of the duplex formed between the antisense and sense nucleic acids, e.g., phosphorothioate derivatives and acridine substituted nucleotides can be used. Examples of modified nucleotides which can be used to generate the antisense nucleic acid include 5-

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fluorouracil, 5-bromouracil, 5-chlorouracil, 5-iodouracil, hypoxanthine, xanthine, 4-acetylcytosine, 5-(carboxyhydroxylmethyl) uracil, 5-carboxymethylaminomethyl-2-thiouridine, 5-carboxymethylaminomethyluracil, dihydrouracil, beta-D-galactosylqueosine, inosine, N6-isopentenyladenine, 1-methylguanine, 1-methylguanine, 2,2-dimethylguanine, 2-methylguanine, 2-methylguanine, 3-methylcytosine, 5-methylguanine, N6-adenine, 7-methylguanine, 5-methylguanine, 5-methylguanine, 5-

methylcytosine, N6-adenine, 7-methylguanine, 5-methylaminomethyluracil, 5-methoxyaminomethyl-2-thiouracil, beta-D-mannosylqueosine, 5'-methoxycarboxymethyluracil, 5-methoxyuracil, 2-methylthio-N6-isopentenyladenine, uracil-5-oxyacetic acid (v), wybutoxosine, pseudouracil, queosine, 2-thiocytosine, 5-methyl-2-thiouracil, 2-thiouracil, 4-thiouracil, 5-methyluracil, uracil-5-oxyacetic acid methylester, uracil-5-oxyacetic acid (v), 5-methyl-2-thiouracil, 3-(3-amino-3-N-2-carboxypropyl) uracil, (acp3)w, and 2,6-diaminopurine. Alternatively, the antisense nucleic acid can be produced biologically using an expression vector into which a nucleic acid has been subcloned in an antisense orientation (*i.e.*, RNA transcribed from the inserted nucleic acid will be of an antisense orientation to a target nucleic acid of interest, described further in the following subsection).

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The antisense nucleic acid molecules of the invention are typically administered to a cell or generated *in situ* such that they hybridize with or bind to cellular mRNA and/or genomic DNA encoding an SRT protein to thereby inhibit expression of the protein, *e.g.*, by inhibiting transcription and/or translation. The hybridization can be by conventional nucleotide complementarity to form a stable duplex, or, for example, in the case of an antisense nucleic acid molecule which binds to DNA duplexes, through specific interactions in the major groove of the double helix. The antisense molecule can be modified such that it specifically binds to a receptor or an antigen expressed on a selected cell surface, *e.g.*, by linking the antisense nucleic acid molecule to a peptide or an antibody which binds to a cell surface receptor or antigen. The antisense nucleic acid molecule can also be delivered to cells using the vectors described herein. To achieve sufficient intracellular concentrations of the antisense molecules, vector constructs in

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which the antisense nucleic acid molecule is placed under the control of a strong prokaryotic, viral, or eukaryotic promoter are preferred.

In yet another embodiment, the antisense nucleic acid molecule of the invention is an α-anomeric nucleic acid molecule. An α-anomeric nucleic acid molecule forms 5 specific double-stranded hybrids with complementary RNA in which, contrary to the usual β-units, the strands run parallel to each other (Gaultier et al. (1987) Nucleic Acids. Res. 15:6625-6641). The antisense nucleic acid molecule can also comprise a 2'-omethylribonucleotide (Inoue et al. (1987) Nucleic Acids Res. 15:6131-6148) or a chimeric RNA-DNA analogue (Inoue et al. (1987) FEBS Lett. 215:327-330).

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In still another embodiment, an antisense nucleic acid of the invention is a ribozyme. Ribozymes are catalytic RNA molecules with ribonuclease activity which are capable of cleaving a single-stranded nucleic acid, such as an mRNA, to which they have a complementary region. Thus, ribozymes (e.g., hammerhead ribozymes (described in Haselhoff and Gerlach (1988) Nature 334:585-591)) can be used to catalytically cleave SRT mRNA transcripts to thereby inhibit translation of SRT mRNA. A ribozyme having specificity for an SRT-encoding nucleic acid can be designed based upon the nucleotide sequence of an SRT cDNA disclosed herein (i.e., SEQ ID NO:119 (RXA00600)). For example, a derivative of a Tetrahymena L-19 IVS RNA can be constructed in which the nucleotide sequence of the active site is complementary to the 20 nucleotide sequence to be cleaved in an SRT-encoding mRNA. See, e.g., Cech et al. U.S. Patent No. 4,987,071 and Cech et al. U.S. Patent No. 5,116,742. Alternatively, SRT mRNA can be used to select a catalytic RNA having a specific ribonuclease activity from a pool of RNA molecules. See, e.g., Bartel, D. and Szostak, J.W. (1993) Science 261:1411-1418.

25 Alternatively, SRT gene expression can be inhibited by targeting nucleotide sequences complementary to the regulatory region of an SRT nucleotide sequence (e.g., an SRT promoter and/or enhancers) to form triple helical structures that prevent transcription of an SRT gene in target cells. See generally, Helene, C. (1991) Anticancer Drug Des. 6(6):569-84; Helene, C. et al. (1992) Ann. N.Y. Acad. Sci. 660:27-36; and Maher, L.J. (1992) Bioassays 14(12):807-15. 30

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B. Recombinant Expression Vectors and Host Cells

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Another aspect of the invention pertains to vectors, preferably expression vectors, containing a nucleic acid encoding an SRT protein (or a portion thereof). As used herein, the term "vector" refers to a nucleic acid molecule capable of transporting another nucleic acid to which it has been linked. One type of vector is a "plasmid", which refers to a circular double stranded DNA loop into which additional DNA segments can be ligated. Another type of vector is a viral vector, wherein additional DNA segments can be ligated into the viral genome. Certain vectors are capable of autonomous replication in a host cell into which they are introduced (e.g., bacterial vectors having a bacterial origin of replication and episomal mammalian vectors). Other vectors (e.g., non-episomal mammalian vectors) are integrated into the genome of a host cell upon introduction into the host cell, and thereby are replicated along with the host genome. Moreover, certain vectors are capable of directing the expression of genes to which they are operatively linked. Such vectors are referred to herein as "expression vectors". In general, expression vectors of utility in recombinant DNA techniques are often in the form of plasmids. In the present specification, "plasmid" and "vector" can be used interchangeably as the plasmid is the most commonly used form of vector. However, the invention is intended to include such other forms of expression vectors, such as viral vectors (e.g., replication defective retroviruses, adenoviruses and adenoassociated viruses), which serve equivalent functions.

The recombinant expression vectors of the invention comprise a nucleic acid of the invention in a form suitable for expression of the nucleic acid in a host cell, which means that the recombinant expression vectors include one or more regulatory sequences, selected on the basis of the host cells to be used for expression, which is operatively linked to the nucleic acid sequence to be expressed. Within a recombinant expression vector, "operably linked" is intended to mean that the nucleotide sequence of interest is linked to the regulatory sequence(s) in a manner which allows for expression of the nucleotide sequence (e.g., in an in vitro transcription/translation system or in a host cell when the vector is introduced into the host cell). The term "regulatory sequence" is intended to include promoters, enhancers and other expression control elements (e.g., polyadenylation signals). Such regulatory sequences are described, for example, in Goeddel; Gene Expression Technology: Methods in Enzymology 185,

Academic Press, San Diego, CA (1990). Regulatory sequences include those which direct constitutive expression of a nucleotide sequence in many types of host cell and those which direct expression of the nucleotide sequence only in certain host cells. Preferred regulatory sequences are, for example, promoters such as cos-, tac-, trp-, tet-, trp-tet-, lpp-, lac-, lpp-lac-, lacI^q-, T7-, T5-, T3-, gal-, trc-, ara-, SP6-, arny, SPO2, λ-P_R- or λ P_L, which are used preferably in bacteria. Additional regulatory sequences are, for example, promoters from yeasts and fungi, such as ADC1, MFα, AC, P-60, CYC1, GAPDH, TEF, rp28, ADH, promoters from plants such as CaMV/35S, SSU, OCS, lib4, usp, STLS1, B33, nos or ubiquitin- or phaseolin-promoters. It is also possible to use artificial promoters. It will be appreciated by one of ordinary skill in the art that the design of the expression vector can depend on such factors as the choice of the host cell to be transformed, the level of expression of protein desired, etc. The expression vectors of the invention can be introduced into host cells to thereby produce proteins or peptides, including fusion proteins or peptides, encoded by nucleic acids as described herein (e.g., SRT proteins, mutant forms of SRT proteins, fusion proteins, etc.).

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The recombinant expression vectors of the invention can be designed for expression of SRT proteins in prokaryotic or eukaryotic cells. For example, SRT genes can be expressed in bacterial cells such as C. glutamicum, insect cells (using baculovirus expression vectors), yeast and other fungal cells (see Romanos, M.A. et al. (1992) 20 "Foreign gene expression in yeast: a review", Yeast 8: 423-488; van den Hondel, C.A.M.J.J. et al. (1991) "Heterologous gene expression in filamentous fungi" in: More Gene Manipulations in Fungi, J.W. Bennet & L.L. Lasure, eds., p. 396-428: Academic Press: San Diego; and van den Hondel, C.A.M.J.J. & Punt, P.J. (1991) "Gene transfer systems and vector development for filamentous fungi, in: Applied Molecular Genetics 25 of Fungi, Peberdy, J.F. et al., eds., p. 1-28, Cambridge University Press: Cambridge), algae and multicellular plant cells (see Schmidt, R. and Willmitzer, L. (1988) High efficiency Agrobacterium tumefaciens -mediated transformation of Arabidopsis thaliana leaf and cotyledon explants" Plant Cell Rep.: 583-586), or mammalian cells. Suitable host cells are discussed further in Goeddel, Gene Expression Technology: Methods in Enzymology 185, Academic Press, San Diego, CA (1990). Alternatively, the recombinant expression vector can be transcribed and translated in vitro, for example using T7 promoter regulatory sequences and T7 polymerase.

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Expression of proteins in prokaryotes is most often carried out with vectors containing constitutive or inducible promoters directing the expression of either fusion or non-fusion proteins. Fusion vectors add a number of amino acids to a protein encoded therein, usually to the amino terminus of the recombinant protein. Such fusion vectors typically serve three purposes: 1) to increase expression of recombinant protein; 2) to increase the solubility of the recombinant protein; and 3) to aid in the purification of the recombinant protein by acting as a ligand in affinity purification. Often, in fusion expression vectors, a proteolytic cleavage site is introduced at the junction of the fusion moiety and the recombinant protein to enable separation of the recombinant protein from the fusion moiety subsequent to purification of the fusion protein. Such enzymes, and their cognate recognition sequences, include Factor Xa, thrombin and enterokinase.

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Typical fusion expression vectors include pGEX (Pharmacia Biotech Inc; Smith, D.B. and Johnson, K.S. (1988) Gene 67:31-40), pMAL (New England Biolabs, Beverly, MA) and pRIT5 (Pharmacia, Piscataway, NJ) which fuse glutathione S-transferase (GST), maltose E binding protein, or protein A, respectively, to the target recombinant protein. In one embodiment, the coding sequence of the SRT protein is cloned into a pGEX expression vector to create a vector encoding a fusion protein comprising, from the N-terminus to the C-terminus, GST-thrombin cleavage site-X protein. The fusion protein can be purified by affinity chromatography using glutathione-agarose resin. Recombinant SRT protein unfused to GST can be recovered by cleavage of the fusion protein with thrombin.

Examples of suitable inducible non-fusion E. coli expression vectors include pTrc (Amann et al., (1988) Gene 69:301-315) pLG338, pACYC184, pBR322, pUC18, pUC19, pKC30, pRep4, pHS1, pHS2, pPLc236, pMBL24, pLG200, pUR290, pIN-III113-B1, \(\lambda\)gt11, pBdCl, and pET 11d (Studier et al., Gene Expression Technology: Methods in Enzymology 185, Academic Press, San Diego, California (1990) 60-89; and Pouwels et al., eds. (1985) Cloning Vectors. Elsevier: New York IBSN 0 444 904018). Target gene expression from the pTrc vector relies on host RNA polymerase transcription from a hybrid trp-lac fusion promoter. Target gene expression from the 30 pET 11d vector relies on transcription from a T7 gn10-lac fusion promoter mediated by a coexpressed viral RNA polymerase (T7 gn1). This viral polymerase is supplied by host strains BL21(DE3) or HMS174(DE3) from a resident λ prophage harboring a T7

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gn1 gene under the transcriptional control of the lacUV 5 promoter. For transformation of other varieties of bacteria, appropriate vectors may be selected. For example, the plasmids pIJ101, pIJ364, pIJ702 and pIJ361 are known to be useful in transforming Streptomyces, while plasmids pUB110, pC194, or pBD214 are suited for transformation of Bacillus species. Several plasmids of use in the transfer of genetic information into Corynebacterium include pHM1519, pBL1, pSA77, or pAJ667 (Pouwels *et al.*, eds. (1985) Cloning Vectors. Elsevier: New York IBSN 0 444 904018).

One strategy to maximize recombinant protein expression is to express the protein in a host bacteria with an impaired capacity to proteolytically cleave the recombinant protein (Gottesman, S., Gene Expression Technology: Methods in Enzymology 185, Academic Press, San Diego, California (1990) 119-128). Another strategy is to alter the nucleic acid sequence of the nucleic acid to be inserted into an expression vector so that the individual codons for each amino acid are those preferentially utilized in the bacterium chosen for expression, such as C. glutamicum (Wada et al. (1992) Nucleic Acids Res. 20:2111-2118). Such alteration of nucleic acid sequences of the invention can be carried out by standard DNA synthesis techniques.

In another embodiment, the SRT protein expression vector is a yeast expression vector. Examples of vectors for expression in yeast *S. cerevisiae* include pYepSec1 (Baldari, *et al.*, (1987) *Embo J.* 6:229-234), 2 μ, pAG-1, Yep6, Yep13, pEMBLYe23, pMFa (Kurjan and Herskowitz, (1982) *Cell* 30:933-943), pJRY88 (Schultz *et al.*, (1987) *Gene* 54:113-123), and pYES2 (Invitrogen Corporation, San Diego, CA). Vectors and methods for the construction of vectors appropriate for use in other fungi, such as the filamentous fungi, include those detailed in: van den Hondel, C.A.M.J.J. & Punt, P.J. (1991) "Gene transfer systems and vector development for filamentous fungi, in: Applied Molecular Genetics of Fungi, J.F. Peberdy, *et al.*, eds., p. 1-28, Cambridge University Press: Cambridge, and Pouwels *et al.*, eds. (1985) Cloning Vectors. Elsevier: New York (IBSN 0 444 904018).

Alternatively, the SRT proteins of the invention can be expressed in insect cells using baculovirus expression vectors. Baculovirus vectors available for expression of proteins in cultured insect cells (e.g., Sf 9 cells) include the pAc series (Smith et al. (1983) Mol. Cell Biol. 3:2156-2165) and the pVL series (Lucklow and Summers (1989) Virology 170:31-39).

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In another embodiment, the SRT proteins of the invention may be expressed in unicellular plant cells (such as algae) or in plant cells from higher plants (e.g., the spermatophytes, such as crop plants). Examples of plant expression vectors include those detailed in: Becker, D., Kemper, E., Schell, J. and Masterson, R. (1992) "New plant binary vectors with selectable markers located proximal to the left border", *Plant Mol. Biol.* 20: 1195-1197; and Bevan, M.W. (1984) "Binary *Agrobacterium* vectors for plant transformation", *Nucl. Acid. Res.* 12: 8711-8721, and include pLGV23, pGHlac+, pBIN19, pAK2004, and pDH51 (Pouwels et al., eds. (1985) Cloning Vectors. Elsevier: New York IBSN 0 444 904018).

In yet another embodiment, a nucleic acid of the invention is expressed in mammalian cells using a mammalian expression vector. Examples of mammalian expression vectors include pCDM8 (Seed, B. (1987) *Nature* 329:840) and pMT2PC (Kaufman *et al.* (1987) *EMBO J.* 6:187-195). When used in mammalian cells, the expression vector's control functions are often provided by viral regulatory elements.

For example, commonly used promoters are derived from polyoma, Adenovirus 2, cytomegalovirus and Simian Virus 40. For other suitable expression systems for both prokaryotic and eukaryotic cells see chapters 16 and 17 of Sambrook, J., Fritsh, E. F., and Maniatis, T. *Molecular Cloning: A Laboratory Manual. 2nd, ed., Cold Spring Harbor Laboratory*, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, 1989.

In another embodiment, the recombinant mammalian expression vector is capable of directing expression of the nucleic acid preferentially in a particular cell type (e.g., tissue-specific regulatory elements are used to express the nucleic acid). Tissue-specific regulatory elements are known in the art. Non-limiting examples of suitable tissue-specific promoters include the albumin promoter (liver-specific; Pinkert et al. (1987) Genes Dev. 1:268-277), lymphoid-specific promoters (Calame and Eaton (1988) Adv. Immunol. 43:235-275), in particular promoters of T cell receptors (Winoto and Baltimore (1989) EMBO J. 8:729-733) and immunoglobulins (Banerji et al. (1983) Cell 33:729-740; Queen and Baltimore (1983) Cell 33:741-748), neuron-specific promoters (e.g., the neurofilament promoter; Byrne and Ruddle (1989) PNAS 86:5473-5477), pancreas-specific promoters (Edlund et al. (1985) Science 230:912-916), and mammary gland-specific promoters (e.g., milk whey promoter; U.S. Patent No. 4,873,316 and

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European Application Publication No. 264,166). Developmentally-regulated promoters are also encompassed, for example the murine hox promoters (Kessel and Gruss (1990) *Science* 249:374-379) and the α -fetoprotein promoter (Campes and Tilghman (1989) *Genes Dev.* 3:537-546).

The invention further provides a recombinant expression vector comprising a DNA molecule of the invention cloned into the expression vector in an antisense orientation. That is, the DNA molecule is operatively linked to a regulatory sequence in a manner which allows for expression (by transcription of the DNA molecule) of an RNA molecule which is antisense to SRT mRNA. Regulatory sequences operatively linked to a nucleic acid cloned in the antisense orientation can be chosen which direct the continuous expression of the antisense RNA molecule in a variety of cell types, for instance viral promoters and/or enhancers, or regulatory sequences can be chosen which direct constitutive, tissue specific or cell type specific expression of antisense RNA. The antisense expression vector can be in the form of a recombinant plasmid, phagemid or attenuated virus in which antisense nucleic acids are produced under the control of a high efficiency regulatory region, the activity of which can be determined by the cell type into which the vector is introduced. For a discussion of the regulation of gene expression using antisense genes see Weintraub, H. et al., Antisense RNA as a molecular tool for genetic analysis, Reviews - Trends in Genetics, Vol. 1(1) 1986.

Another aspect of the invention pertains to host cells into which a recombinant expression vector of the invention has been introduced. The terms "host cell" and "recombinant host cell" are used interchangeably herein. It is understood that such terms refer not only to the particular subject cell but to the progeny or potential progeny of such a cell. Because certain modifications may occur in succeeding generations due to either mutation or environmental influences, such progeny may not, in fact, be identical to the parent cell, but are still included within the scope of the term as used herein.

A host cell can be any prokaryotic or eukaryotic cell. For example, an SRT protein can be expressed in bacterial cells such as *C. glutamicum*, insect cells, yeast or mammalian cells (such as Chinese hamster ovary cells (CHO) or COS cells). Other suitable host cells are known to those of ordinary skill in the art. Microorganisms related

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to *Corynebacterium glutamicum* which may be conveniently used as host cells for the nucleic acid and protein molecules of the invention are set forth in Table 3.

Vector DNA can be introduced into prokaryotic or eukaryotic cells via conventional transformation or transfection techniques. As used herein, the terms "transformation" and "transfection" are intended to refer to a variety of art-recognized techniques for introducing foreign nucleic acid (e.g., linear DNA or RNA (e.g., a linearized vector or a gene construct alone without a vector) or nucleic acid in the form of a vector (e.g., a plasmid, phage, phasmid, phagemid, transposon or other DNA)) into a host cell, including calcium phosphate or calcium chloride co-precipitation, DEAE-dextran-mediated transfection, lipofection, or electroporation. Suitable methods for transforming or transfecting host cells can be found in Sambrook, et al. (Molecular Cloning: A Laboratory Manual. 2nd, ed., Cold Spring Harbor Laboratory, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, 1989), and other laboratory manuals.

For stable transfection of mammalian cells, it is known that, depending upon the expression vector and transfection technique used, only a small fraction of cells may integrate the foreign DNA into their genome. In order to identify and select these integrants, a gene that encodes a selectable marker (e.g., resistance to antibiotics) is generally introduced into the host cells along with the gene of interest. Preferred selectable markers include those which confer resistance to drugs, such as G418, hygromycin and methotrexate. Nucleic acid encoding a selectable marker can be introduced into a host cell on the same vector as that encoding an SRT protein or can be introduced on a separate vector. Cells stably transfected with the introduced nucleic acid can be identified by drug selection (e.g., cells that have incorporated the selectable marker gene will survive, while the other cells die).

To create a homologous recombinant microorganism, a vector is prepared which contains at least a portion of an SRT gene into which a deletion, addition or substitution has been introduced to thereby alter, e.g., functionally disrupt, the SRT gene.

Preferably, this SRT gene is a Corynebacterium glutamicum SRT gene, but it can be a homologue from a related bacterium or even from a mammalian, yeast, or insect source.

In a preferred embodiment, the vector is designed such that, upon homologous recombination, the endogenous SRT gene is functionally disrupted (i.e., no longer encodes a functional protein; also referred to as a "knock out" vector). Alternatively,

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the vector can be designed such that, upon homologous recombination, the endogenous SRT gene is mutated or otherwise altered but still encodes functional protein (e.g., the upstream regulatory region can be altered to thereby alter the expression of the endogenous SRT protein). In the homologous recombination vector, the altered portion of the SRT gene is flanked at its 5' and 3' ends by additional nucleic acid of the SRT gene to allow for homologous recombination to occur between the exogenous SRT gene carried by the vector and an endogenous SRT gene in a microorganism. The additional flanking SRT nucleic acid is of sufficient length for successful homologous recombination with the endogenous gene. Typically, several kilobases of flanking DNA (both at the 5' and 3' ends) are included in the vector (see e.g., Thomas, K.R., and Capecchi, M.R. (1987) Cell 51: 503 for a description of homologous recombination vectors). The vector is introduced into a microorganism (e.g., by electroporation) and cells in which the introduced SRT gene has homologously recombined with the endogenous SRT gene are selected, using art-known techniques.

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In another embodiment, recombinant microorganisms can be produced which contain selected systems which allow for regulated expression of the introduced gene. For example, inclusion of an SRT gene on a vector placing it under control of the lac operon permits expression of the SRT gene only in the presence of IPTG. Such regulatory systems are well known in the art.

In another embodiment, an endogenous SRT gene in a host cell is disrupted (e.g., by homologous recombination or other genetic means known in the art) such that expression of its protein product does not occur. In another embodiment, an endogenous or introduced SRT gene in a host cell has been altered by one or more point mutations, deletions, or inversions, but still encodes a functional SRT protein. In still another embodiment, one or more of the regulatory regions (e.g., a promoter, repressor, or inducer) of an SRT gene in a microorganism has been altered (e.g., by deletion, truncation, inversion, or point mutation) such that the expression of the SRT gene is modulated. One of ordinary skill in the art will appreciate that host cells containing more than one of the described SRT gene and protein modifications may be readily produced using the methods of the invention, and are meant to be included in the present invention.

A host cell of the invention, such as a prokaryotic or eukaryotic host cell in culture, can be used to produce (*i.e.*, express) an SRT protein. Accordingly, the invention further provides methods for producing SRT proteins using the host cells of the invention. In one embodiment, the method comprises culturing the host cell of invention (into which a recombinant expression vector encoding an SRT protein has been introduced, or into which genome has been introduced a gene encoding a wild-type or altered SRT protein) in a suitable medium until SRT protein is produced. In another embodiment, the method further comprises isolating SRT proteins from the medium or the host cell.

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C. Isolated SRT Proteins

Another aspect of the invention pertains to isolated SRT proteins, and biologically active portions thereof. An "isolated" or "purified" protein or biologically active portion thereof is substantially free of cellular material when produced by recombinant DNA techniques, or chemical precursors or other chemicals when chemically synthesized. The language "substantially free of cellular material" includes preparations of SRT protein in which the protein is separated from cellular components of the cells in which it is naturally or recombinantly produced. In one embodiment, the language "substantially free of cellular material" includes preparations of SRT protein having less than about 30% (by dry weight) of non-SRT protein (also referred to herein as a "contaminating protein"), more preferably less than about 20% of non-SRT protein, still more preferably less than about 10% of non-SRT protein, and most preferably less than about 5% non-SRT protein. When the SRT protein or biologically active portion thereof is recombinantly produced, it is also preferably substantially free of culture medium, i.e., culture medium represents less than about 20%, more preferably less than about 10%, and most preferably less than about 5% of the volume of the protein preparation. The language "substantially free of chemical precursors or other chemicals" includes preparations of SRT protein in which the protein is separated from chemical precursors or other chemicals which are involved in the synthesis of the protein. In one embodiment, the language "substantially free of chemical precursors or other chemicals" includes preparations of SRT protein having less than about 30% (by dry weight) of chemical precursors or non-SRT chemicals, more preferably less than

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about 20% chemical precursors or non-SRT chemicals, still more preferably less than about 10% chemical precursors or non-SRT chemicals, and most preferably less than about 5% chemical precursors or non-SRT chemicals. In preferred embodiments, isolated proteins or biologically active portions thereof lack contaminating proteins from the same organism from which the SRT protein is derived. Typically, such proteins are produced by recombinant expression of, for example, a *C. glutamicum* SRT protein in a microorganism such as *C. glutamicum*.

An isolated SRT protein or a portion thereof of the invention can contribute to the resistance or tolerance of C. glutamicum to one or more chemical or environmental stresses or hazards, or has one or more of the activities set forth in Table 1. In preferred embodiments, the protein or portion thereof comprises an amino acid sequence which is sufficiently homologous to an amino acid sequence of the invention (e.g., a sequence of an even-numbered SEQ ID NO: of the Sequence Listing) such that the protein or portion thereof maintains the ability to mediate the resistance or tolerance of C. glutamicum to one or more chemical or environmental stresses or hazards. The portion of the protein is preferably a biologically active portion as described herein. In another preferred embodiment, an SRT protein of the invention has an amino acid sequence set forth as an even-numbered SEQ ID NO: of the Sequence Listing. In yet another preferred embodiment, the SRT protein has an amino acid sequence which is encoded by a nucleotide sequence which hybridizes, e.g., hybridizes under stringent conditions, to a nucleotide sequence of the invention (e.g., a sequence of an odd-numbered SEQ ID NO: of the Sequence Listing). In still another preferred embodiment, the SRT protein has an amino acid sequence which is encoded by a nucleotide sequence that is at least about 50%, 51%, 52%, 53%, 54%, 55%, 56%, 57%, 58%, 59%, or 60%, preferably at least about 61%, 62%, 63%, 64%, 65%, 66%, 67%, 68%, 69%, or 70%, more preferably at least about 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, or 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, or 90%, or 91%, 92%, 93%, 94%, and even more preferably at least about 95%, 96%, 97%, 98%, 99% or more homologous to one of the nucleic acid sequences of the invention, or a portion thereof. Ranges and identity values intermediate to the above-recited values, (e.g., 70-90% identical or 80-95% identical) are also intended to be encompassed by the present invention. For example, ranges of identity values using a combination of any of the above values recited as upper

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and/or lower limits are intended to be included. The preferred SRT proteins of the present invention also preferably possess at least one of the SRT activities described herein. For example, a preferred SRT protein of the present invention includes an amino acid sequence encoded by a nucleotide sequence which hybridizes, *e.g.*, hybridizes under stringent conditions, to a nucleotide sequence of the invention, and which can increase the resistance or tolerance of C. glutamicum to one or more environmental or chemical stresses, or which has one or more of the activities set forth in Table 1.

In other embodiments, the SRT protein is substantially homologous to an amino acid sequence of the invention (e.g., a sequence of an even-numbered SEQ ID NO: of the Sequence Listing) and retains the functional activity of the protein of one of the amino acid sequences of the invention yet differs in amino acid sequence due to natural variation or mutagenesis, as described in detail in subsection I above. Accordingly, in another embodiment, the SRT protein is a protein which comprises an amino acid sequence which is at least about 50%, 51%, 52%, 53%, 54%, 55%, 56%, 57%, 58%, 59%, or 60%, preferably at least about 61%, 62%, 63%, 64%, 65%, 66%, 67%, 68%, 69%, or 70%, more preferably at least about 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, or 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, or 90%, or 91%, 92%, 93%, 94%, and even more preferably at least about 95%, 96%, 97%, 98%, 99% or more homologous to an entire amino acid sequence of the invention and which has at least one of the SRT activities described herein. Ranges and identity values intermediate to the above-recited values, (e.g., 70-90% identical or 80-95% identical) are also intended to be encompassed by the present invention. For example, ranges of identity values using a combination of any of the above values recited as upper and/or lower limits are intended to be included. In another embodiment, the invention pertains to a full length C. glutamicum protein which is substantially homologous to an entire amino acid sequence of the invention.

Biologically active portions of an SRT protein include peptides comprising amino acid sequences derived from the amino acid sequence of an SRT protein, e.g., an amino acid sequence of an even-numbered SEQ ID NO: of the Sequence Listing or the amino acid sequence of a protein homologous to an SRT protein, which include fewer amino acids than a full length SRT protein or the full length protein which is homologous to an SRT protein, and exhibit at least one activity of an SRT protein.

Typically, biologically active portions (peptides, e.g., peptides which are, for example, 5, 10, 15, 20, 30, 35, 36, 37, 38, 39, 40, 50, 100 or more amino acids in length) comprise a domain or motif with at least one activity of an SRT protein. Moreover, other biologically active portions, in which other regions of the protein are deleted, can be prepared by recombinant techniques and evaluated for one or more of the activities described herein. Preferably, the biologically active portions of an SRT protein include one or more selected domains/motifs or portions thereof having biological activity.

SRT proteins are preferably produced by recombinant DNA techniques. For example, a nucleic acid molecule encoding the protein is cloned into an expression vector (as described above), the expression vector is introduced into a host cell (as described above) and the SRT protein is expressed in the host cell. The SRT protein can then be isolated from the cells by an appropriate purification scheme using standard protein purification techniques. Alternative to recombinant expression, an SRT protein, polypeptide, or peptide can be synthesized chemically using standard peptide synthesis techniques. Moreover, native SRT protein can be isolated from cells (*e.g.*, endothelial cells), for example using an anti-SRT antibody, which can be produced by standard techniques utilizing an SRT protein or fragment thereof of this invention.

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The invention also provides SRT chimeric or fusion proteins. As used herein, an SRT "chimeric protein" or "fusion protein" comprises an SRT polypeptide operatively linked to a non-SRT polypeptide. An "SRT polypeptide" refers to a polypeptide having an amino acid sequence corresponding to SRT, whereas a "non-SRT polypeptide" refers to a polypeptide having an amino acid sequence corresponding to a protein which is not substantially homologous to the SRT protein, *e.g.*, a protein which is different from the SRT protein and which is derived from the same or a different organism. Within the fusion protein, the term "operatively linked" is intended to indicate that the SRT polypeptide and the non-SRT polypeptide are fused in-frame to each other. The non-SRT polypeptide can be fused to the N-terminus or C-terminus of the SRT polypeptide. For example, in one embodiment the fusion protein is a GST-SRT fusion protein in which the SRT sequences are fused to the C-terminus of the GST sequences. Such fusion proteins can facilitate the purification of recombinant SRT proteins. In another embodiment, the fusion protein is an SRT protein containing a heterologous signal sequence at its N-terminus. In certain host cells (*e.g.*, mammalian host cells), expression

and/or secretion of an SRT protein can be increased through use of a heterologous signal sequence.

Preferably, an SRT chimeric or fusion protein of the invention is produced by standard recombinant DNA techniques. For example, DNA fragments coding for the different polypeptide sequences are ligated together in-frame in accordance with conventional techniques, for example by employing blunt-ended or stagger-ended termini for ligation, restriction enzyme digestion to provide for appropriate termini, filling-in of cohesive ends as appropriate, alkaline phosphatase treatment to avoid undesirable joining, and enzymatic ligation. In another embodiment, the fusion gene can be synthesized by conventional techniques including automated DNA synthesizers. Alternatively, PCR amplification of gene fragments can be carried out using anchor primers which give rise to complementary overhangs between two consecutive gene fragments which can subsequently be annealed and reamplified to generate a chimeric gene sequence (see, for example, Current Protocols in Molecular Biology, eds. Ausubel et al. John Wiley & Sons: 1992). Moreover, many expression vectors are commercially available that already encode a fusion moiety (e.g., a GST polypeptide). An SRTencoding nucleic acid can be cloned into such an expression vector such that the fusion moiety is linked in-frame to the SRT protein.

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Homologues of the SRT protein can be generated by mutagenesis, e.g., discrete point mutation or truncation of the SRT protein. As used herein, the term "homologue" refers to a variant form of the SRT protein which acts as an agonist or antagonist of the activity of the SRT protein. An agonist of the SRT protein can retain substantially the same, or a subset, of the biological activities of the SRT protein. An antagonist of the SRT protein can inhibit one or more of the activities of the naturally occurring form of the SRT protein, by, for example, competitively binding to a downstream or upstream member of the SRT system which includes the SRT protein. Thus, the C. glutamicum SRT protein and homologues thereof of the present invention may increase the tolerance or resistance of C. glutamicum to one or more chemical or environmental stresses.

In an alternative embodiment, homologues of the SRT protein can be identified by screening combinatorial libraries of mutants, e.g., truncation mutants, of the SRT protein for SRT protein agonist or antagonist activity. In one embodiment, a variegated library of SRT variants is generated by combinatorial mutagenesis at the nucleic acid

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level and is encoded by a variegated gene library. A variegated library of SRT variants can be produced by, for example, enzymatically ligating a mixture of synthetic oligonucleotides into gene sequences such that a degenerate set of potential SRT sequences is expressible as individual polypeptides, or alternatively, as a set of larger fusion proteins (e.g., for phage display) containing the set of SRT sequences therein. There are a variety of methods which can be used to produce libraries of potential SRT homologues from a degenerate oligonucleotide sequence. Chemical synthesis of a degenerate gene sequence can be performed in an automatic DNA synthesizer, and the synthetic gene then ligated into an appropriate expression vector. Use of a degenerate set of genes allows for the provision, in one mixture, of all of the sequences encoding the desired set of potential SRT sequences. Methods for synthesizing degenerate oligonucleotides are known in the art (see, e.g., Narang, S.A. (1983) Tetrahedron 39:3; Itakura et al. (1984) Annu. Rev. Biochem. 53:323; Itakura et al. (1984) Science 198:1056; Ike et al. (1983) Nucleic Acid Res. 11:477.

In addition, libraries of fragments of the SRT protein coding can be used to generate a variegated population of SRT fragments for screening and subsequent selection of homologues of an SRT protein. In one embodiment, a library of coding sequence fragments can be generated by treating a double stranded PCR fragment of an SRT coding sequence with a nuclease under conditions wherein nicking occurs only about once per molecule, denaturing the double stranded DNA, renaturing the DNA to form double stranded DNA which can include sense/antisense pairs from different nicked products, removing single stranded portions from reformed duplexes by treatment with S1 nuclease, and ligating the resulting fragment library into an expression vector. By this method, an expression library can be derived which encodes N-terminal, C-terminal and internal fragments of various sizes of the SRT protein.

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Several techniques are known in the art for screening gene products of combinatorial libraries made by point mutations or truncation, and for screening cDNA libraries for gene products having a selected property. Such techniques are adaptable for rapid screening of the gene libraries generated by the combinatorial mutagenesis of SRT homologues. The most widely used techniques, which are amenable to high through-put analysis, for screening large gene libraries typically include cloning the gene library into replicable expression vectors, transforming appropriate cells with the resulting library of

vectors, and expressing the combinatorial genes under conditions in which detection of a desired activity facilitates isolation of the vector encoding the gene whose product was detected. Recursive ensemble mutagenesis (REM), a new technique which enhances the frequency of functional mutants in the libraries, can be used in combination with the screening assays to identify SRT homologues (Arkin and Yourvan (1992) *PNAS* 89:7811-7815; Delgrave *et al.* (1993) *Protein Engineering* 6(3):327-331).

In another embodiment, cell based assays can be exploited to analyze a variegated SRT library, using methods well known in the art.

10 D. Uses and Methods of the Invention

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The nucleic acid molecules, proteins, protein homologues, fusion proteins, primers, vectors, and host cells described herein can be used in one or more of the following methods: identification of *C. glutamicum* and related organisms; mapping of genomes of organisms related to *C. glutamicum*; identification and localization of *C. glutamicum* sequences of interest; evolutionary studies; determination of SRT protein regions required for function; modulation of an SRT protein activity; modulation of the activity of an SRT pathway; and modulation of cellular production of a desired compound, such as a fine chemical.

The SRT nucleic acid molecules of the invention have a variety of uses. First, they may be used to identify an organism as being *Corynebacterium glutamicum* or a close relative thereof. Also, they may be used to identify the presence of *C. glutamicum* or a relative thereof in a mixed population of microorganisms. The invention provides the nucleic acid sequences of a number of *C. glutamicum* genes; by probing the extracted genomic DNA of a culture of a unique or mixed population of microorganisms under stringent conditions with a probe spanning a region of a *C. glutamicum* gene which is unique to this organism, one can ascertain whether this organism is present.

Although Corynebacterium glutamicum itself is nonpathogenic, it is related to pathogenic species, such as Corynebacterium diphtheriae. Corynebacterium diphtheriae is the causative agent of diphtheria, a rapidly developing, acute, febrile infection which involves both local and systemic pathology. In this disease, a local lesion develops in the upper respiratory tract and involves necrotic injury to epithelial cells; the bacilli secrete toxin which is disseminated through this lesion to distal susceptible tissues of the

body. Degenerative changes brought about by the inhibition of protein synthesis in these tissues, which include heart, muscle, peripheral nerves, adrenals, kidneys, liver and spleen, result in the systemic pathology of the disease. Diphtheria continues to have high incidence in many parts of the world, including Africa, Asia, Eastern Europe and the independent states of the former Soviet Union. An ongoing epidemic of diphtheria in the latter two regions has resulted in at least 5,000 deaths since 1990.

In one embodiment, the invention provides a method of identifying the presence or activity of *Cornyebacterium diphtheriae* in a subject. This method includes detection of one or more of the nucleic acid or amino acid sequences of the invention (e.g., the sequences set forth as odd-numbered or even-numbered SEQ ID NOs, respectively, in the Sequence Listing) in a subject, thereby detecting the presence or activity of *Corynebacterium diphtheriae* in the subject. *C. glutamicum* and *C. diphtheriae* are related bacteria, and many of the nucleic acid and protein molecules in *C. glutamicum* are homologous to *C. diphtheriae* nucleic acid and protein molecules, and can therefore be used to detect *C. diphtheriae* in a subject.

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The nucleic acid and protein molecules of the invention may also serve as markers for specific regions of the genome. This has utility not only in the mapping of the genome, but also for functional studies of *C. glutamicum* proteins. For example, to identify the region of the genome to which a particular *C. glutamicum* DNA-binding protein binds, the *C. glutamicum* genome could be digested, and the fragments incubated with the DNA-binding protein. Those which bind the protein may be additionally probed with the nucleic acid molecules of the invention, preferably with readily detectable labels; binding of such a nucleic acid molecule to the genome fragment enables the localization of the fragment to the genome map of *C. glutamicum*, and, when performed multiple times with different enzymes, facilitates a rapid determination of the nucleic acid sequence to which the protein binds. Further, the nucleic acid molecules of the invention may be sufficiently homologous to the sequences of related species such that these nucleic acid molecules may serve as markers for the construction of a genomic map in related bacteria, such as *Brevibacterium lactofermentum*.

The SRT nucleic acid molecules of the invention are also useful for evolutionary and protein structural studies. The resistance processes in which the molecules of the invention participate are utilized by a wide variety of cells; by comparing the sequences

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of the nucleic acid molecules of the present invention to those encoding similar enzymes from other organisms, the evolutionary relatedness of the organisms can be assessed. Similarly, such a comparison permits an assessment of which regions of the sequence are conserved and which are not, which may aid in determining those regions of the protein which are essential for the functioning of the enzyme. This type of determination is of value for protein engineering studies and may give an indication of what the protein can tolerate in terms of mutagenesis without losing function.

The genes of the invention, e.g., the gene encoding LMRB (SEQ ID NO:1) or other gene of the invention encoding a chemical or environmental resistance or tolerance protein (e.g., resistance against one or more antibiotics), may be used as genetic markers for the genetic transformation of (e.g., the transfer of additional genes into or disruption of preexisting genes of) organisms such as C. glutamicum or other bacterial species. Use of these nucleic acid molecules permits efficient selection of organisms which have incorporated a given transgene cassette (e.g., a plasmid, phage, phasmid, phagemid, transposon, or other nucleic acid element), based on a trait which permits the survival of the organism in an otherwise hostile or toxic environment (e.g., in the presence of an antimicrobial compound). By employing one or more of the genes of the invention as genetic markers, the speed and ease with which organisms having desirable transformed traits (e.g., modulated fine chemical production) are engineered and isolated are improved. While it is advantageous to use the genes of the invention for selection of transformed C. glutamicum and related bacteria, it is possible, as described herein, to use homologs (e.g., homologs from other organisms), allelic variants or fragments of the gene retaining desired activity. Furthermore, 5' and 3' regulatory elements of the genes of the invention may be modified as described herein (e.g., by nucleotide substitution, insertion, deletion, or replacement with a more desirable genetic element) to modulate the transcription of the gene. For example, an LMRB variant in which the nucleotide sequence in the region from -1 to -200 5' to the start codon has been altered to modulate (preferably increase) the transcription and/or translation of LMRB may be employed, as can constructs in which a gene of the invention (e.g., the LMRB gene (SEQ ID NO:1)) is functionally coupled to one or more regulatory signals (e.g., inducer or repressor binding sequences) which can be used for modulating gene expression.

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Similarly, more than one copy of a gene (functional or inactivated) of the invention may be employed.

An additional application of the genes of the invention (e.g., the gene encoding LMRB (SEQ ID NO:1) or other drug- or antibiotic-resistance gene) is in the discovery of new antibiotics which are active against Corynebacteria and/or other bacteria. For example, a gene of the invention may be expressed (or overexpressed) in a suitable host to generate an organism with increased resistance to one or more drugs or antibiotics (in the case of LMRB, lincosamides in particular, especially lincomycin). This type of resistant host can subsequently be used to screen for chemicals with bacteriostatic and/or bacteriocidal activity, such as novel antibiotic compounds. It is possible, in particular, to use the genes of the invention (e.g., the LMRB gene) to identify new antibiotics which are active against those microorganisms which are already resistant to standard antibiotic compounds.

The invention provides methods for screening molecules which modulate the activity of an SRT protein, either by interacting with the protein itself or a substrate or binding partner of the SRT protein, or by modulating the transcription or translation of SRT nucleic acid molecule of the invention. In such methods, a microorganism expressing one or more SRT proteins of the invention is contacted with one or more test compounds, and the effect of each test compound on the activity or level of expression of the SRT protein is assessed.

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Manipulation of the SRT nucleic acid molecules of the invention may result in the production of SRT proteins having functional differences from the wild-type SRT proteins. These proteins may be improved in efficiency or activity, may be present in greater numbers in the cell than is usual, or may be decreased in efficiency or activity. The goal of such manipulations is to increase the viability and activity of the cell when the cell is exposed to the environmental and chemical stresses and hazards which frequently accompany large-scale fermentative culture. Thus, by increasing the activity or copy number of a heat-shock-regulated protease, one may increase the ability of the cell to destroy incorrectly folded proteins, which may otherwise interfere with normal cellular functioning (for example, by continuing to bind substrates or cofactors although the protein lacks the activity to act on these molecules appropriately). The same is true for the overexpression or optimization of activity of one or more chaperone molecules

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induced by heat or cold shock. These proteins aid in the correct folding of nascent polypeptide chains, and thus their increased activity or presence should increase the percentage of correctly folded proteins in the cell, which in turn should increase the overall metabolic efficiency and viability of the cells in culture. The overexpression or optimization of the transporter molecules activated by osmotic shock should result in an increased ability on the part of the cell to maintain intracellular homeostasis, thereby increasing the viability of these cells in culture. Similarly, the overproduction or increase in activity by mutagenesis of proteins involved in the development of cellular resistance to chemical stresses of various kinds (either by transport of the offending chemical out of the cell or by modification of the chemical to a less hazardous substance) should increase the fitness of the organism in the environment containing the hazardous substance (i.e., large-scale fermentative culture), and thereby may permit relatively larger numbers of cells to survive in such a culture. The net effect of all of these mutagenesis strategies is to increase the quantity of fine-chemical-producing compounds in the culture, thereby increasing the yield, production, and/or efficiency of production of one or more desired fine chemicals from the culture.

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This aforementioned list of mutagenesis strategies for SRT proteins to result in increased yields of a desired compound is not meant to be limiting; variations on these mutagenesis strategies will be readily apparent to one of ordinary skill in the art. By these mechanisms, the nucleic acid and protein molecules of the invention may be utilized to generate *C. glutamicum* or related strains of bacteria expressing mutated SRT nucleic acid and protein molecules such that the yield, production, and/or efficiency of production of a desired compound is improved. This desired compound may be any natural product of *C. glutamicum*, which includes the final products of biosynthesis pathways and intermediates of naturally-occurring metabolic pathways, as well as molecules which do not naturally occur in the metabolism of *C. glutamicum*, but which are produced by a *C. glutamicum* strain of the invention.

This invention is further illustrated by the following examples which should not be construed as limiting. The contents of all references, patent applications, patents, published patent applications, Tables, and the sequence listing cited throughout this application are hereby incorporated by reference.

TABLE 1: Genes Included in the Application

Eunction Lincomycine RESISTANCE PROTEIN 10 KD CHAPERONIN 60 KD CHAPERONIN 60 KD CHAPERONIN CATALASE (EC 1.11.1.6) CATALASE (EC 1.11.1.6) CARBON STARVATION PROTEIN A SUPEROXIDE DISMUTASE [MN] (EC 1.15.1.1) SUPEROXIDE DISMUTASE [MN] (EC 1.15.1.1) PHOSPHINOTHRICIN-RESISTANCE PROTEIN PHOSPHINOTHRICIN-RESISTANCE PROTEIN	,	Function	Moleculares chaperon (HSP70/DnaK family)	Molecular chaperones (HSP70/DnaK family)	DNAJ PROTEIN	GRPE PROTEIN	DNAK PROTEIN	DNAK PROTEIN	TRAP1	Molecular chaperone, HSP90 family	DNAJ PROTEIN	TRIGGER FACTOR	PS1 PROTEIN VORLÄUFER	PS1 PROTEIN VORLÄUFER	PS1 PROTEIN VORLÄUFER	PSI PROTEIN VORLAUTER DRA DROTEIN VORLÄLIERR	PREPROTEIN TRANSLOKASE SECE UNTEREINHEIT	PREPROTEIN TRANSLOKASE SECA UNTEREINHEIT	PROTEIN-EXPORT MEMBRANE PROTEIN SECD	Signal Erkennung particle GTPase	/O/C Thioredoxin-ähnliche oxidoreductase	THIOL PEROXIDASE (EC 1.11.1)
NT Stop 30483 348 16002 1601 203 5865 594 87476 15252	!	NT Stop	3432	9	12473	13865	20178	14522	92	1480	13541	1582	43666	631	1069	3300 3486	31575	13749	5954	6058	24	8533
NT Start 29041 52 14389 363 802 7412 7412 7412 8087 14716 2130		NT Start	4883	1172	13657	14518	22031	16375	1849	1145	12396	2928	42941	2	761	2032 1906	31243	11932	7795	5363	1172	8039
Contig. GR00424 CR00124 VV0086 GR00129 GR00159 GR00159 VV0098 VV0098 VV0098 GR00156	:	Contig	W0123	GR00391	GR00726	GR00726	VV0057	GR00726	VV0152	GR00659	GR00242	W0251	VV0017	VV0018	W0018	VV0022 VV0026	VV0025	W0124	W0171	W0119	VV0206	VV0180
Identification Code RXA01524 RXA00497 RXN00493 F RXA00498 RXA01217 RXA001217 RXA003119 RXN03119 RXN03120 RXN03575 F RXA00575	;	Identification Code	RXN01345	F RXA01345	RXA02541	RXA02542	RXN02543	F RXA02543	RXN02280	F RXA02282	RXA00886	RXS00568	RXN03038	RXN03039	RXN03040	RXN03054	RXN02949	RXN02462	RXN01559	RXN00046	RXN01863	RXN00833
Amino Acid SEQ ID NO 2 2 4 4 6 6 6 11 0 12 14 4 14 18 20 22 22	les .	Amino Acid SEQ ID NO	24	56	28	30	32	34	36	38	40	42	4	46	8 4	22 25	5 2	56	58	09	62	64
Nucleic Acid SEQ ID NO 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	Chaperones	Nucleic Acid	23	25	27	29	31	33	35	37	39	41	43	45	47	51.0	53	55	57	59	61	63

	Function	THIOL: DISULFIDE AUSTAUSCH PROTEIN DSBD THIOL: DISULFIDE AUSTAUSCH PROTEIN TLPA	THIOREDOXIN	THIOREDOXIN	PEPTIDYL-PROLYL CIS-TRANS ISOMERASE (EC 5.2.1.8)	PEPTID KETTE RELEASE FACTOR 3	PEPTID KETTE RELEASE FACTOR 3	PUTATIVES OXPPCYCLE PROTEIN OPCA	SMALL COLD-SHOCK PROTEIN SMALL COLD-SHOCK PROTEIN		Function	COLD SHOCK-LIKE PROTEIN CSPC	SMALL COLD-SHOCK PROTEIN	PROBABLE HYDROGEN PEROXIDE-INDUCIBLE GENES ACTIVATOR	damage-inducible protein P	Object TOOLER INDOCIDES TROUBLE TROUBL	GTP PYROPHOSPHOKINASE (EC 2.7.6.5)	LYTB PROTEIN	DIADENOSINE 5',5"-P1,P4-TETRAPHOSPHATE HYDROLASE (EC 3.6.1.17)	DIADENOSINE 5',5"-P1,P4-TETRAPHOSPHATE HYDROLASE (EC 3.6.1.17)	EXCONDENSITY OF THE STATE OF TH	GOANOVINE-3, 3-813(DIPTOVITATE) 3-PYROPHOVITIONYORYORYUKOLAVE (EC. 3.1.7.2) EKOPOLYPHONPHATANE (EC. 3.6.1.11)	EXOPOLYPHOSPHATASE (EC 3.6.1.11)		<u>Function</u>	ARGININE HYDROXIMATE RESISTANCE PROTEIN	ARSENATE REDUCTASE	ARSENICAL-RESISTANCE PROTEIN ACR3	ARSENICAL-RESISTANCE PROTEIN ACR3	ARSENICAL-RESISTANCE PROTEIN ACR3	BACH MASSIN RESISTANCE PROTEIN (POINTING UNDECAPRENDE NINASE) (EC 2.7.1.00) BICYCLOMYCIN RESISTANCE PROTEIN
led)	NT Stop	11304 216	42706	6393	7879	741	518	14556	3665		NT Stop	19248	895	2771	1192	1633	4017	706	6768	16749	4//7	16535	2353		NT Stop	6743	6199	1457	5760	6916	3201
Table 1 (continued)	NT Start	12059 836	42335	5527	7103	-	141	13600	3465		NT Start	19628	792	1878	11640	551	3388	1680	5761	17276	5259	15609	2763		NT Start	6231	5837	1843	4651	6278	4052
Table	Contig.	VV0179 VV0223	VV0079	VV0047	VV0320	VV0284	W0111	VV0074	GR00549	nses	Contig.	GR00641	GR00218	GR00467	GR00708	GR00709	GR00276	VV0321	W0143	VV0050	VV0319	VV0043	W0319		Contig.	GR00640	GR00646	GR00159	GR00646	GR00646	GR00245
	Identification Code	RXN01676 RXN00380	RXN00937	RXN02325	RXN01837	RXN01926	RXN02002	RXN02736	RXS03217 F RXA01917	Proteins involved in stress respor	Identification Code	RXA02184	RXA00810	RXA01674	EXA02431	RXA02861	RXA00981	RXN00786	RXS01027	RXS01528	AX3017.15	RXS02497	RXS02972	erance	Identification Code	RXA02159	RXA02201	RXA00599 RXA00600	RXA02200	RXA02202	RXA00900
	Amino Acid SEQ ID NO	99 89	02	72	74	92	78	80	82 84	involved i	Amino Acid SEO ID NO	86	88	06	26	t 8	86	100	102	104	9 9	110	112	Resistance and tolerance	Amino Acid	114	116	120	122	124 126	128
	Nucleic Acid SEQ ID NO	65 67	69	71	73	75	77	79	83	Proteins i	Nucleic Acid	85	87	60	91	S &	97	66	5	103	5 5	109	Ξ	Resistano	Nucleic Acid		115	119	121	123 125	127

		BICYCLOMYCIN RESISTANCE PROTEIN	BICYCLOMYCIN RESISTANCE PROTEIN	CHLORAMPHENICOL RESISTANCE PROTEIN	CHECKAMPHENICOL MENIN PARCHEN CHI ORAMPHENICOL MENINTANCE PROTEIN	COPPER RESISTANCE PROTEIN C PRECURSOR	COPPER RESISTANCE PROTEIN C PRECURSOR	DAUNORUBICIN RESISTANCE ATP-BINDING PROTEIN DRRA	DAUNORUBICIN RESISTANCE PROTEIN	DAUNORUBICIN RESISTANCE PROTEIN	DAUNORUBICIN RESISTANCE PROTEIN	RESISTANCE TRANSMEMBRANE PROTEIN	METHYLENOMYCIN A RESISTANCE PROTEIN	METHYLENOMYCIN A RESISTANCE PROTEIN	METHYLENOMYCIN A KESISTANCE PROTEIN	METHYLENOMYCIN A RESISTANCE PROTEIN	METHYLENOMYCIN A RESISTANCE PROTEIN	MYCINAMICIN-RESISTANCE PROTEIN MYRA	.UX PROTEIN	NCE PROTEIN	ICE PROTEIN	QUINOLONE RESISTANCE NORA PROTEIN	QUINOLONE RESISTANCE NORA PROTEIN	STANCE NORA PROTEIN	QUINOLONE RESISTANCE NORA PROTEIN	STANCE NORA PROTEIN	QUINOLONE RESISTANCE NORA PROTEIN	DATINOMYCIN CLA HYDROXY AND	VIBRIOBACTIN UTILIZATION PROTEIN VIUB	CTASE	MERCURIC REDUCTASE (EC 1.16.1.1)	CTASE (EC 1.16.1.1)	MERCORIC REDUCTION (EC. 1.16.1.1) HEAVY METAL TO EBANDE DECITED DEFICIENCE	HEAVY METAL TOLERANCE PROTEIN PRECURSOR	VANZ PROTEIN, teicoplanin resistance protein	Resistance Protein	Resistance Protein	MULTIDRUG RESISTANCE PROTEIN B	Resistance Protein	Drug Transporter	ransporter	Drug Transporter	Drug Transporter	ransporter
	Function	BICYCLOMYCIN R	BICYCLOMYCIN R	CHLORAMPHENIC	CHLORAMPHENIC	COPPER RESISTA	COPPER RESISTA	DAUNORUBICIN R	DAUNORUBICIN R	DAUNORUBICIN R	DAUNORUBICIN R	DAUNORUBICIN R	METHYLENOMYCI	METHYLENOMYCI	MEIHYLENOMYC	METHYLENOMYCI	METHYLENOMYCI	MYCINAMICIN-RE	MACROLIDE-EFFLUX PROTEIN	NICKEL RESISTANCE PROTEIN	NICKEL RESISTANCE PROTEIN	QUINOLONE RESI	QUINOLONE RESI	QUINOLONE RESI	QUINOLONE RESI	QUINOLONE RESI	CONOCONE REST	DAINOMYCIN C-1	VIBRIOBACTIN UT	ARSENATE REDUCTASE	MERCURIC REDU(MERCURIC REDUC	MERCORIC REDUC	HEAVY METAL TO	VANZ PROTEIN, to	Hypothetical Drug Resistance Protein	Hypothetical Drug Resistance Protein	MULTIDRUG RESI	Hypothetical Drug Resistance Protein	Hypothetical Drug T	Hypothetical Drug Transporter	Hypothetical Drug T	Hypothetical Drug T	Hypothetical Orug Transporter
(panu	NT Stop	8168	3980	4438	181	565	565	1023	5611	256	2025	283	52629	5162	3028	4184 4184	1109	339	41387	8975	9821	4894	4	4612	2917	6714	2147	2070	1543	3580	3706	4191	1245	9	2690	819	1946	18381	9005	3216	2120	14101	963	765
Table 1 (continued)	NT Start	8581	4357	3263	282	1176	1176	1763	7950	7	463	1023	53858	4560	3918	4384 2034		. –	40116	9626	10246	3776	774	5754	3807	7931	1680	252	2367	3236	3398	3772	808	641	3298	2054	855	16933	8058	2491	1395	16290	4	4
Table	Contig	VV0140	GR00245	GR00046	6R00574	GR00015	GR00015	GR00283	VV0180	GR00224	GR00225	GR00283	6000	GR00214	GR00410	GK00410	GR00552	GR00626	VV0127	GR00555	GR00555	VV0209	GR00288	VV0136	GR00323	VV0102	GROUBSB	GROOFES	GR00013	GR00228	GR00296	GR00296	VV0106	GR00282	GR00296	VV0248	GR00535	02000	GR00655	VV0042	GR10044	GR00119	VV0108	GR00336
	Identification Code	RXN00901	F RXA00901	RXA00289	F RXA01984	RXA00109	RXA00109	RXA00996	RXN00829	F RXA00829	F RXA00834	RXA00995	RXN00803	F RXA00803	FXA01407	RXA01408	F RXA01922	RXA02060	RXN01936	F RXA01936	F RXA01937	EXN01010	F RXA01010	RXN03142	F KXA01150	KXN02964	P KANZI 15	RXA02305	RXA00084	RXA00843	RXA01052	EXA01053	RXN03123	F RXA00993	RXA01051	RXN01873	F RXA01873	RXN00034	F RXA02273	RXN03075	F RXA02907	RXA00479	EXN03124	F RXA01180
	Amino Acid		132	134 136	138	140	142	144	146	148	150	152	154	156 158	200		164	166	168	170	172	174	176	178	08.5	182	5 4 5 4	188	190	192	194	500	200	202	204	506	208	210	212	214	216	218	220	77.7
	Nucleic Acid	129	131	133	137	139	141	143	145	147	149	151	153	155	2.5	161	163	165	167	169	171	173	175	17	6/1	101	185	187	189	191	193	195	199	201	203	205	207	209	211	213	215	217	219	177

			Table	able 1 (continued)	ed)	
Nucleic Acid	SEO ID NO	dentification Code	Contig.	NT Start	NT Stop	Function
223	224	RXA02586	GR00741	10296	10027	Hypothetical Drug Transporter
225	226	RXA02587	GR00741	12343	10253	Hypothetical Drug Transporter
227	228	RXN03042	VV0018	2440	1835	Hypothetical Drug Transporter
229	230	F RXA02893	GR10035	1841	1236	Hypothetical Drug Transporter
231	232	RXA01616	GR00450	1684	203	MÜLTIDRUG EFFLUX PROTEIN QACB
ဗ	234	RXA01666	GR00463	2307	3683	MULTIDRUG RESISTANCE PROTEIN
235	236	RXA00062	GR00009	13252	11855	MULTIDRUG RESISTANCE PROTEIN B
237	238	RXA00215	GR00032	13834	15294	
239	240	RXN03064	VV0038	4892	6223	MULTIDRUG RESISTANCE PROTEIN B
•	242	F RXA00565	GR00151	4892	5884	MULTIDRUG RESISTANCE PROTEIN B
243	244	F RXA02878	GR10016	1837	1481	MULTIDRUG RESISTANCE PROTEIN B
245	246	RXA00648	GR00169	2713	1304	MULTIDRUG RESISTANCE PROTEIN B
247	248	RXN01320	VV0082	13146	11500	MULTIDRUG RESISTANCE PROTEIN B
249	250	F RXA01314	GR00382	744	4	MULTIDRUG RESISTANCE PROTEIN B
251	252	F RXA01320	GR00383	1979	1200	MULTIDRUG RESISTANCE PROTEIN B
e	254	RXN02926	VV0082	11497	9866	MULTIDRUG RESISTANCE PROTEIN B
255	256	F RXA01319	GR00383	1197	4	MULTIDRUG RESISTANCE PROTEIN B
	258	RXA01578	GR00439	1423	29	MULTIDRUG RESISTANCE PROTEIN B
259	260	RXA02087	GR00629	7076	5730	MULTIDRUG RESISTANCE PROTEIN B
261	262	RXA02088	GR00629	8294	7080	MULTIDRUG RESISTANCE PROTEIN B
263	264	RXA00764	GR00204	3284	2169	BMRU PROTEIN Bacillus subtilis bmrU, multidruq efflux transporter
	266	RXN03125	VV0108	972	1142	Hypothetical Drug Transporter
	268	RXN01553	VV0135	25201	26520	Hypothetical Drug Permease
•	270	RXN00535	VV0219	5155	5871	Hypothetical Drug Resistance Protein
271	272	RXN00453	0000	1173	3521	Hypothetical Drug Transporter
~	274	RXN00932	W0171	13120	13593	Hypothetical Drug Transporter
.0	276	RXN03022	VV0002	65	511	MULTIDRUG RESISTANCE PROTEIN B
277	278	RXN03151	VV0163	489	4	MYCINAMICIN-RESISTANCE PROTEIN MYRA
Φ.	280	RXN02832	VV0358	547	2	LYSOSTAPHIN IMMUNITY FACTOR
_	282	RXN00165	VV0232	3275	1860	MULTIDRUG RESISTANCE-LIKE ATP-BINDING PROTEIN MOL
m	284	RXN01190	VV0169	8992	10338	MULTIDRUG RESISTANCE-LIKE ATP-BINDING PROTEIN MDL
285	286	RXN01102	VV0059	6128	4884	QUINOLONE RESISTANCE NORA PROTEIN
~	288	RXN00788	VV0321	3424	3648	CHLORAMPHENICOL RESISTANCE PROTEIN
289	290	RXN02119	VV0102	11242	9602	A201A-RESISTANCE ATP-BINDING PROTEIN
_	292	RXN01605	VV0137	7124	5610	DAUNORUBICIN RESISTANCE TRANSMEMBRANE PROTEIN
293	294	RXN01091	VV0326	267	4	MAZG PROTEIN
ω Ω	296	RXS02979	VV0149	2150	2383	MERCURIC TRANSPORT PROTEIN PERIPLASMIC COMPONENT PRECURSOR
297	298	RXS02987	VV0234	527	294	MERCURIC TRANSPORT PROTEIN PERIPLASMIC COMPONENT PRECURSOR
299	300	RXS03095	VV0057	4056	4424	CADMIUM EFFLUX SYSTEM ACCESSORY PROTEIN HOMOLOG

		TABLE 2 - Excluded Genes	ded Genes
GenBank TM Accession No.	Gene Name	Gene Function	Reference
A09073	gdd	Phosphoenol pyruvate carboxylase	Bachmann, B. et al. "DNA fragment coding for phosphoenolpyruvat corboxylase, recombinant DNA carrying said fragment, strains carrying the recombinant DNA and method for producing L-aminino acids using said strains," Patent: EP 0358940-A 3 03/21/90
A45579, A45581, A45583, A45585 A45587		Threonine dehydratase	Moeckel, B. et al. "Production of L-isoleucine by means of recombinant micro-organisms with deregulated threonine dehydratase," Patent: WO 9519442-A 5 07/20/95
AB003132	murC; ftsQ; ftsZ		Kobayashi, M. et al. "Cloning, sequencing, and characterization of the ftsZ gene from coryneform bacteria," Biochem. Biophys. Res. Commun., 236(2):383-388 (1997)
AB015023	murC; ftsQ		Wachi, M. et al. "A murC gene from Coryneform bacteria," Appl. Microbiol. Biotechnol., 51(2):223-228 (1999)
AB018530	dtsR		Kimura, E. et al. "Molecular cloning of a novel gene, dtsR, which rescues the detergent sensitivity of a mutant derived from <i>Brevibacterium</i> lactofermentum," Biosci. Biotechnol. Biochem., 60(10): 1565-1570 (1996)
AB018531	dtsR1; dtsR2		
AB020624	muri	D-glutamate racemase	
AB023377	tkt	transketolase	
AB024708	gltB; gltD	Glutamine 2-oxoglutarate aminotransferase large and small subunits	
AB025424	acn	aconitase	
AB027714	rep	Replication protein	
AB027715	rep; aad	Replication protein; aminoglycoside adenyltransferase	
AF005242	argC	N-acety/glutamate-5-semialdehyde dehydrogenase	
AF005635	glnA	Glutamine synthetase	
AF030405	hisF	cyclase	
AF030520	argG	Argininosuccinate synthetase	
AF031518	argF	Ornithine carbamolytransferase	
AF036932	aroD	3-dehydroquinate dehydratase	
AF038548	pyc	Pyruvate carboxylase	

AF038651 AF041436 AF045998 AF048964 AF049897	dciAE; apt; rel argR impA argH argC; argJ; argB; argD; argF; argR; argG; argH	Table 2 (continued) Dipeptide-binding protein; adenine phosphoribosyltransferase; GTP (p)pp pyrophosphokinase Arginine repressor Inositol monophosphate phosphatase Argininosuccinate lyase N-acetylglutamylphosphate reductase; ornithine acetyltransferase; N-acetylglutamate kinase; acetylomithine transminase; ornithine carbamoyltransferase; arginine repressor;	Wehmeier, L. et al. "The role of the Corynebacterium glutamicum rel gene in (p)ppGpp metabolism," <i>Microbiology</i> , 144:1853-1862 (1998)
AF050109 AF050166 AF051846 AF052652	inhA hisG hisA metA	argininosuccinate lyase Enoyl-acyl carrier protein reductase ATP phosphoribosyltransferase Phosphoribosylformimino-5-amino-1- phosphoribosyl-4-imidazolecarboxamide isomerase Homoserine O-acetyltransferase	Park, S. et al. "Isolation and analysis of metA, a methionine biosynthetic gene encoding homoserine acetyltransferase in Corynebacterium glutamicum," Mol.
AF053071 AF060558 AF086704 AF114233	aroB hisH hisE aroA	Dehydroquinate synthetase Glutamine amidotransferase Phosphoribosyl-ATP- pyrophosphohydrolase 5-enolpyruvylshikimate 3-phosphate	Cells., 8(3):286-294 (1998)
AF116184 AF124518	panD aroD; aroE	L-aspartate-alpha-decarboxylase precursor 3-dehydroquinase, shikimate	Dusch, N. et al. "Expression of the Corynebacterium glutamicum panD gene encoding L-aspartate-alpha-decarboxylase leads to pantothenate overproduction in Escherichia coli," <i>Appl. Environ. Microbiol.</i> , 65(4)1530-1539 (1999)
AF124600 AF145897 AF145898	aroC; aroK; aroB; pepQ inhA inhA	denydrogenase Chorismate synthase; shikimate kinase; 3- dehydroquinate synthase; putative cytoplasmic peptidase	

		Table 2 (continued)	nued)
AJ001436	ectP	Transport of ectoine, glycine betaine, proline	Peter, H. et al. "Corynebacterium glutamicum is equipped with four secondary carriers for compatible solutes: Identification, sequencing, and characterization of the proline/ectoine uptake system, ProP, and the ectoine/proline/glycine betaine carrier, EctP," J. Bacteriol., 180(22):6005-6012 (1998)
AJ004934	барD	Tetrahydrodipicolinate succinylase (incomplete')	Wehrmann, A. et al. "Different modes of diaminopimelate synthesis and their role in cell wall integrity: A study with Corynebacterium glutamicum," J. Bacteriol., 180(12):3159-3165 (1998)
AJ007732	ppc; secG; amt; ocd; soxA	Phosphoenolpyruvate-carboxylase; ?; high affinity ammonium uptake protein; putative ornithine-cyclodecarboxylase; sarcosine oxidase	
AJ010319	ftsY, glnB, glnD; srp; amtP	Involved in cell division; PII protein; uridylyltransferase (uridylyl-removing enzmye); signal recognition particle; low affinity ammonium uptake protein	Jakoby, M. et al. "Nitrogen regulation in Corynebacterium glutamicum; Isolation of genes involved in biochemical characterization of corresponding proteins," FEMS Microbiol., 173(2):303-310 (1999)
AJ132968	cat	Chloramphenicol aceteyl transferase	
AJ224946	тдо	L-malate: quinone oxidoreductase	Molenaar, D. et al. "Biochemical and genetic characterization of the membrane-associated malate dehydrogenase (acceptor) from Corynebacterium glutamicum," Eur. J. Biochem, 254(2):395-403 (1998)
AJ238250	hudh	NADH dehydrogenase	
AJ238703	porA	Porin	Lichtinger, T. et al. "Biochemical and biophysical characterization of the cell wall porin of Corynebacterium glutamicum: The channel is formed by a low molecular mass polypeptide," <i>Biochemistry</i> , 37(43):15024-15032 (1998)
D17429		Transposable element IS31831	Vertes et al. "Isolation and characterization of IS31831, a transposable element from Corynebacterium glutamicum," Mol. Microbiol., 11(4):739-746 (1994)
D84102	odhA	2-oxoglutarate dehydrogenase	Usuda, Y. et al. "Molecular cloning of the Corynebacterium glutamicum (Brevibacterium lactofermentum AJ12036) odhA gene encoding a novel type of 2-oxoglutarate dehydrogenase," <i>Microbiology</i> , 142:3347-3354 (1996)
E01358	hdh; hk	Homoserine dehydrogenase; homoserine kinase	Katsumata, R. et al. "Production of L-thereonine and L-isoleucine," Patent: JP 1987232392-A 1 10/12/87
E01359		Upstream of the start codon of homoserine kinase gene	Katsumata, R. et al. "Production of L-thereonine and L-isoleucine," Patent: JP 1987232392-A 2 10/12/87
E01375		Tryptophan operon	
E01376	трЬ; трЕ	Leader peptide; anthranilate synthase	Matsui, K. et al. "Tryptophan operon, peptide and protein coded thereby, utilization of tryptophan operon gene expression and production of tryptophan," Patent: JP 1987244382-A 1 10/24/87

	Table 7 (continued)	nned)
E01377	Promoter and operator regions of tryptophan operon	Matsui, K. et al. "Tryptophan operon, peptide and protein coded thereby, utilization of tryptophan operon gene expression and production of tryptophan:" Patent: JP 1987244382-A 10/24/87
E03937	Biotin-synthase	Hatakeyama, K. et al. "DNA fragment containing gene capable of coding biotin synthetase and its utilization," Patent: JP 1992278088-A 1 10/02/92
E04040	Diamino pelargonic acid aminotransferase	Kohama, K. et al. "Gene coding diaminopelargonic acid aminotransferase and desthiobiotin synthetase and its utilization," Patent: JP 1992330284-A 1 11/18/92
E04041	Desthiobiotinsynthetase	Kohama, K. et al. "Gene coding diaminopelargonic acid aminotransferase and desthiobiotin synthetase and its utilization," Patent: JP 1992330284-A 111/18/92
E04307	Flavum aspartase	Kurusu, Y. et al. "Gene DNA coding aspartase and utilization thereof," Patent: JP 1993030977-A 1 02/09/93
E04376	socitric acid lyase	Katsumata, R. et al. "Gene manifestation controlling DNA," Patent: JP 1993056782-A 3 03/09/93
E04377	Isocitric acid lyase N-terminal fragment	Katsumata, R. et al. "Gene manifestation controlling DNA," Patent: JP 1993056782-A 3 03/09/93
E04484	Prephenate dehydratase	Sotouchi, N. et al. "Production of L-phenylalanine by fermentation," Patent: JP 1993076352-A 2 03/30/93
E05108	Aspartokinase	Fugono, N. et al. "Gene DNA coding Aspartokinase and its use," Patent: JP 1993184366-A 1 07/27/93
E05112	Dihydro-dipichorinate synthetase	Hatakeyama, K. et al. "Gene DNA coding dihydrodipicolinic acid synthetase and its use," Patent: JP 1993184371-A 1 07/27/93
E05776	Diaminopimelic acid dehydrogenase	Kobayashi, M. et al. "Gene DNA coding Diaminopimelic acid dehydrogenase and its use," Patent: JP 1993284970-A 1 11/02/93
E05779	Threonine synthase	Kohama, K. et al. "Gene DNA coding threonine synthase and its use," Patent: JP 1993284972-A 1 11/02/93
E06110	Prephenate dehydratase	Kikuchi, T. et al. "Production of L-phenylalanine by fermentation method," Patent: JP 1993344881-A 1 12/27/93
E06111	Mutated Prephenate dehydratase	Kikuchi, T. et al. "Production of L-phenylalanine by fermentation method," Patent: JP 199334881-A 1 12/27/93
E06146	Acetohydroxy acid synthetase	Inui, M. et al. "Gene capable of coding Acetohydroxy acid synthetase and its use," Patent: JP 1993344893-A 1 12/27/93
E06825	Aspartokinase	Sugimoto, M. et al. "Mutant aspartokinase gene," patent: JP 1994062866-A 1 03/08/94
E06826	Mutated aspartokinase alpha subunit	Sugimoto, M. et al. "Mutant aspartokinase gene," patent: JP 1994062866-A 1 03/08/94

		Table 2 (continued)	nued)
E06827		Mutated aspartokinase alpha subunit	Sugimoto, M. et al. "Mutant aspartokinase gene," patent: JP 1994062866-A 1 03/08/94
E07701	secY		Honno, N. et al. "Gene DNA participating in integration of membraneous protein to membrane," Patent: JP 1994169780-A 1 06/21/94
E08177		Aspartokinase	Sato, Y. et al. "Genetic DNA capable of coding Aspartokinase released from feedback inhibition and its utilization," Patent: JP 1994261766-A 1 09/20/94
E08178, E08179, E08180, E08181, E08182		Feedback inhibition-released Aspartokinase	Sato, Y. et al. "Genetic DNA capable of coding Aspartokinase released from feedback inhibition and its utilization," Patent: JP 1994261766-A 1 09/20/94
E08232		Acetohydroxy-acid isomeroreductase	Inui, M. et al. "Gene DNA coding acetohydroxy acid isomeroreductase," Patent: JP 1994277067-A 1 10/04/94
E08234	secE		Asai, Y. et al. "Gene DNA coding for translocation machinery of protein," Patent: JP 1994277073-A 1 10/04/94
E08643		FT aminotransferase and desthiobiotin synthetase promoter region	Hatakeyama, K. et al. "DNA fragment having promoter function in coryneform bacterium," Patent: JP 1995031476-A 1 02/03/95
E08646		Biotin synthetase	Hatakeyama, K. et al. "DNA fragment having promoter function in coryneform bacterium," Patent: JP 1995031476-A 1 02/03/95
E08649		Aspartase	Kohama, K. et al "DNA fragment having promoter function in coryneform bacterium," Patent: JP 1995031478-A 1 02/03/95
E08900		Dihydrodipicolinate reductase	Madori, M. et al. "DNA fragment containing gene coding Dihydrodipicolinate acid reductase and utilization thereof," Patent: JP 1995075578-A 1 03/20/95
E08901		Diaminopimelic acid decarboxylase	Madori, M. et al. "DNA fragment containing gene coding Diaminopimelic acid decarboxylase and utilization thereof," Patent: JP 1995075579-A 1 03/20/95
E12594		Serine hydroxymethyltransferase	Hatakeyama, K. et al. "Production of L-trypophan," Patent: JP 1997028391-A 1 02/04/97
E12760, E12759, E12758		transposase	Moriya, M. et al. "Amplification of gene using artificial transposon," Patent: JP 1997070291-A 03/18/97
E12764		Arginyl-tRNA synthetase; diaminopimelic acid decarboxylase	Moriya, M. et al. "Amplification of gene using artificial transposon," Patent: JP 1997070291-A 03/18/97
E12767		Dihydrodipicolinic acid synthetase	Moriya, M. et al. "Amplification of gene using artificial transposon," Patent: JP 1997070291-A 03/18/97
E12770		aspartokinase	Moriya, M. et al. "Amplification of gene using artificial transposon," Patent: JP 1997070291-A 03/18/97
E12773		Dihydrodipicolinic acid reductase	Moriya, M. et al. "Amplification of gene using artificial transposon," Patent: JP 1997070291-A 03/18/97

		Table 2 (continued)	nued)
E13655		:-6-phosphate dehyd	Hatakeyama, K. et al. "Glucose-6-phosphate dehydrogenase and DNA capable of coding the same," Patent: JP 1997224661-A 1 09/02/97
L01508	llvA	Threonine dehydratase	Moeckel, B. et al. "Functional and structural analysis of the threonine dehydratase of Corynebacterium glutamicum," J. Bacteriol., 174:8065-8072 (1992)
L07603	EC 4.2.1.15	3-deoxy-D-arabinoheptulosonate-7- phosphate synthase	Chen, C. et al. "The cloning and nucleotide sequence of Corynebacterium glutamicum 3-deoxy-D-arabinoheptulosonate-7-phosphate synthase gene," FEMS Microbiol. Lett., 107:223-230 (1993)
L09232	IIvB; iIvN; iIvC	Acetohydroxy acid synthase large subunit; Acetohydroxy acid synthase small subunit; Acetohydroxy acid isomeroreductase	Keilhauer, C. et al. "Isoleucine synthesis in Corynebacterium glutamicum: molecular analysis of the ilvB-ilvN-ilvC operon," J. Bacteriol., 175(17):5595-5603 (1993)
L 18874	PtsM	Phosphoenolpyruvate sugar phosphotransferase	Fouet, A et al. "Bacillus subtilis sucrose-specific enzyme II of the phosphotransferase system: expression in Escherichia coli and homology to enzymes II from enteric bacteria," PNAS USA, 84(24):8773-8777 (1987); Lee, J.K. et al. "Nucleotide sequence of the gene encoding the Corynebacterium glutamicum mannose enzyme II and analyses of the deduced protein sequence," FEMS Microbiol. Lett., 119(1-2):137-145 (1994)
L27123	aceB	Malate synthase	Lee, H-S. et al. "Molecular characterization of aceB, a gene encoding malate synthase in Corynebacterium glutamicum," J. Microbiol. Biotechnol., 4(4):256-263 (1994)
L27126		Pyruvate kinase	Jetten, M. S. et al. "Structural and functional analysis of pyruvate kinase from Corynebacterium glutamicum," <i>Appl. Environ. Microbiol.</i> , 60(7):2501-2507 (1994)
L28760	aceA	Isocitrate lyase	
L35906	dtxr	Diphtheria toxin repressor	Oguiza, J.A. et al. "Molecular cloning, DNA sequence analysis, and characterization of the Corynebacterium diphtheriae dtxR from Brevibacterium lactofermentum," J. Bacteriol, 177(2):465-467 (1995)
M13774		Prephenate dehydratase	Follettie, M.T. et al. "Molecular cloning and nucleotide sequence of the Corynebacterium glutamicum pheA gene," J. Bacteriol, 167:695-702 (1986)
M16175	5S rRNA		Park, Y-H. et al. "Phylogenetic analysis of the coryneform bacteria by 56 rRNA sequences," J. Bacteriol, 169:1801-1806 (1987)
M16663	trpE	Anthranilate synthase, 5° end	Sano, K. et al. "Structure and function of the trp operon control regions of Brevibacterium lactofermentum, a glutamic-acid-producing bacterium," <i>Gene</i> , 52:191-200 (1987)
M16664	trpA	Tryptophan synthase, 3'end	Sano, K. et al. "Structure and function of the trp operon control regions of Brevibacterium lactofermentum, a glutamic-acid-producing bacterium," Gene, 52:191-200 (1987)

		Table 2 (continued)	nued)
M25819		Phosphoenolpyruvate carboxylase	O'Regan, M. et al. "Cloning and nucleotide sequence of the Phosphoenolpyruvate carboxylase-coding gene of Corynebacterium glutamicum ATCC13032," Gene, 77(2):237-251 (1989)
M85106		23S rRNA gene insertion sequence	Roller, C. et al. "Gram-positive bacteria with a high DNA G+C content are characterized by a common insertion within their 23S rRNA genes," J. Gen. Microbiol., 138:1167-1175 (1992)
M85107, M85108		23S rRNA gene insertion sequence	Roller, C. et al. "Gram-positive bacteria with a high DNA G+C content are characterized by a common insertion within their 23S rRNA genes," J. Gen. Microbiol., 138:1167-1175 (1992)
M89931	aecD; brnQ; yhbw	Beta C-S Iyase; branched-chain amino acid uptake carrier; hypothetical protein yhbw	Rossol, I. et al. "The Corynebacterium glutamicum aecD gene encodes a C-S lyase with alpha, beta-elimination activity that degrades aminoethylcysteine," J. Bacteriol., 174(9):2968-2977 (1992); Tauch, A. et al. "Isoleucine uptake in Corynebacterium glutamicum ATCC 13032 is directed by the brnQ gene product," Arch. Microbiol., 169(4):303-312 (1998)
S59299	цъ	Leader gene (promoter)	Herry, D.M. et al. "Cloning of the trp gene cluster from a tryptophan-hyperproducing strain of Corynebacterium glutamicum: identification of a mutation in the trp leader sequence," <i>Appl. Environ. Microbiol.</i> , 59(3):791-799 (1993)
U11545	ιτρ	Anthranilate phosphoribosyltransferase	O'Gara, J.P. and Dunican, L.K. (1994) Complete nucleotide sequence of the Corynebacterium glutamicum ATCC 21850 tpD gene." Thesis, Microbiology Department, University College Galway, Ireland.
U13922	cgliM; cgliR; clgliR	Putative type II 5-cytosoine methyltransferase; putative type II restriction endonuclease; putative type I or type III restriction endonuclease	Schafer, A. et al. "Cloning and characterization of a DNA region encoding a stress-sensitive restriction system from Corynebacterium glutamicum ATCC 13032 and analysis of its role in intergeneric conjugation with Escherichia coli," <i>J. Bacteriol.</i> , 176(23):7309-7319 (1994); Schafer, A. et al. "The Corynebacterium glutamicum cgllM gene encoding a 5-cytosine in an McrBC-deficient Escherichia coli strain," <i>Gene</i> , 203(2):95-101 (1997)
U14965	recA		
U31224	xdd		Ankri, S. et al. "Mutations in the Corynebacterium glutamicumproline biosynthetic pathway: A natural bypass of the proA step," J. Bacteriol., 178(15):4412-4419 (1996)
U3122 <i>5</i>	proC	L-proline: NADP+ 5-oxidoreductase	Ankri, S. et al. "Mutations in the Corynebacterium glutamicumproline biosynthetic pathway: A natural bypass of the proA step," J. Bacteriol., 178(15):4412-4419 (1996)
U31230	obg; proB; unkdh	?;gamma glutamyl kinase;similar to D- isomer specific 2-hydroxyacid dehydrogenases	Ankri, S. et al. "Mutations in the Corynebacterium glutamicumproline biosynthetic pathway: A natural bypass of the proA step," J. Bacteriol., 178(15):4412-4419 (1996)

		Table 2 (continued	(pent
U31281	bioB	ynthase	Serebriiskii, I.G., "Two new members of the bio B superfamily: Cloning, sequencing and expression of bio B genes of Methylobacillus flagellatum and Corynebacterium glutamicum," Gene, 175:15-22 (1996)
U35023	thtR; accBC	Thiosulfate sulfurtransferase, acyl CoA carboxylase	Jager, W. et al. "A Corynebacterium glutamicum gene encoding a two-domain protein similar to biotin carboxylases and biotin-carboxyl-carrier proteins," <i>Arch. Microbiol.</i> , 166(2);76-82 (1996)
U43535	cmr	Multidrug resistance protein	Jager, W. et al. "A Corynebacterium glutamicum gene conferring multidrug resistance in the heterologous host Escherichia coli," J. Bacteriol., 179(7):2449-2451 (1997)
U43536	clpB	Heat shock ATP-binding protein	
U53587	aphA-3	3'5"-aminoglycoside phosphotransferase	
U89648		Corynebacterium glutamicum unidentified sequence involved in histidine biosynthesis, partial sequence	
X04960	trpA; trpB; trpC; trpD; trpE; trpG; trpL	Tryptophan operon	Matsui, K. et al. "Complete nucleotide and deduced amino acid sequences of the Brevibacterium lactofermentum tryptophan operon," <i>Nucleic Acids Res.</i> , 14(24):10113-10114 (1986)
X07563	lys A	DAP decarboxylase (meso-diaminopimelate decarboxylase, EC 4.1.1.20)	Yeh, P. et al. "Nucleic sequence of the lysA gene of Corynebacterium glutamicum and possible mechanisms for modulation of its expression," Mol. Gen. Genet., 212(1):112-119 (1988)
X14234	EC 4.1.1.31	Phosphoenolpyruvate carboxylase	Eikmanns, B.J. et al. "The Phosphoenolpyruvate carboxylase gene of Corynebacterium glutamicum: Molecular cloning, nucleotide sequence, and expression," Mol. Gen. Genet., 218(2):330-339 (1989); Lepiniec, L. et al. "Sorghum Phosphoenolpyruvate carboxylase gene family: structure, function and molecular evolution," Plant. Mol. Biol., 21 (3):487-502 (1993)
X17313	fda	Fructose-bisphosphate aldolase	Von der Osten, C.H. et al. "Molecular cloning, nucleotide sequence and fine- structural analysis of the Corynebacterium glutamicum fda gene: structural comparison of C. glutamicum fructose-1, 6-biphosphate aldolase to class I and class II aldolases," Mol. Microbiol.
X53993	dapA	L-2, 3-dihydrodipicolinate synthetase (EC 4.2.1.52)	Bonnassie, S. et al. "Nucleic sequence of the dapA gene from Corynebacterium glutamicum," Nucleic Acids Res., 18(21):6421 (1990)
X54223		AttB-related site	Cianciotto, N. et al. "DNA sequence homology between att B-related sites of Corynebacterium diphtheriae, Corynebacterium ulcerans, Corynebacterium glutamicum, and the att Site of lambdacorynephage," FEMS. Microbiol, Lett., 66:299-302 (1990)
X54740	argS; lysA	Arginyl-tRNA synthetase; Diaminopimelate decarboxylase	Marcel, T. et al. "Nucleotide sequence and organization of the upstream region of the Corynebacterium glutamicum lysA gene," Mol. Microbiol., 4(11):1819-1830 (1990)

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X55994	trpL; trpE	Putative leader peptide; anthranilate synthase component 1	Heery, D.M. et al. "Nucleotide sequence of the Corynebacterium glutamicum trpE gene," Nucleic Acids Res., 18(23):7138 (1990)
X56037	thrC	Threonine synthase	Han, K.S. et al. "The molecular structure of the Corynebacterium glutamicum threonine synthase gene," Mol. Microbiol., 4(10):1693-1702 (1990)
X56075	attB-related site	Attachment site	Cianciotto, N. et al. "DNA sequence homology between att B-related sites of Corynebacterium diphtheriae, Corynebacterium ulcerans, Corynebacterium glutamicum, and the attP site of lambdacorynephage," FEMS. Microbiol, Lett., 66:299-302 (1990)
X57226	lysC-alpha; lysC-beta; asd	Aspartokinase-alpha subunit; Aspartokinase-beta subunit; aspartate beta semialdehyde dehydrogenase	Kalinowski, J. et al. "Genetic and biochemical analysis of the Aspartokinase from Corynebacterium glutamicum," <i>Mol. Microbiol.</i> , 5(5):1197-1204 (1991); Kalinowski, J. et al. "Aspartokinase genes lysC alpha and lysC beta overlap and are adjacent to the aspertate beta-semialdehyde dehydrogenase gene asd in Corynebacterium glutamicum," <i>Mol. Gen. Genet.</i> , 224(3):317-324 (1990)
X59403	gap;pgk; tpi	Glyceraldehyde-3-phosphate; phosphoglycerate kinase; triosephosphate isomerase	Eikmanns, B.J. "Identification, sequence analysis, and expression of a Corynebacterium glutamicum gene cluster encoding the three glycolytic enzymes glyceraldehyde-3-phosphate dehydrogenase, 3-phosphoglycerate kinase, and triosephosphate isomeras," J. Bacteriol., 174(19):6076-6086 (1992)
X59404	gdh	Glutamate dehydrogenase	Bormann, E.R. et al. "Molecular analysis of the Corynebacterium glutamicum gdh gene encoding glutamate dehydrogenase," Mol. Microbiol., 6(3):317-326 (1992)
X60312	lysI	L-lysine permease	Seep-Feldhaus, A.H. et al. "Molecular analysis of the Corynebacterium glutamicum lysl gene involved in lysine uptake," Mol. Microbiol., 5(12):2995-3005 (1991)
X66078	cop l	Ps1 protein	Joliff, G. et al. "Cloning and nucleotide sequence of the csp1 gene encoding PS1, one of the two major secreted proteins of Corynebacterium glutamicum: The deduced N-terminal region of PS1 is similar to the Mycobacterium antigen 85 complex," Mol. Microbiol., 6(16):2349-2362 (1992)
X66112	glt	Citrate synthase	Eikmanns, B.J. et al. "Cloning sequence, expression and transcriptional analysis of the Corynebacterium glutamicum gltA gene encoding citrate synthase," <i>Microbiol.</i> , 140:1817-1828 (1994)
X67737 X69103	dapB csp2	Dihydrodipicolinate reductase Surface layer protein PS2	Peyret, J.L. et al. "Characterization of the cspB gene encoding PS2, an ordered surface-layer protein in Corynebacterium glutamicum," Mol. Microbiol., 9(1):97-109 (1993)
X69104		IS3 related insertion element	Bonamy, C. et al. "Identification of IS1206, a Corynebacterium glutamicum IS3-related insertion sequence and phylogenetic analysis," Mol. Microbiol., 14(3):571-581 (1994)

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X70959	leuA	Isopropylmalate synthase	Patek, M. et al. "Leucine synthesis in Corynebacterium glutamicum: enzyme activities, structure of leuA, and effect of leuA inactivation on lysine synthesis," Appl. Environ. Microbiol., 60(1):133-140 (1994)
X71489	<u>p</u> 3	Isocitrate dehydrogenase (NADP+)	Eikmanns, B.J. et al. "Cloning sequence analysis, expression, and inactivation of the Corynebacterium glutamicum icd gene encoding isocitrate dehydrogenase and biochemical characterization of the enzyme," J. Bacteriol., 177(3):774-782 (1995)
X72855	GDHA	Glutamate dehydrogenase (NADP+)	
X75083, X70584	mtrA	5-methyltryptophan resistance	Heery, D.M. et al. "A sequence from a tryptophan-hyperproducing strain of Corynebacterium glutamicum encoding resistance to 5-methyltryptophan," Biochem. Biophys. Res. Commun., 201(3):1255-1262 (1994)
X75085	recA		Fitzpatrick, R. et al. "Construction and characterization of recA mutant strains of Corynebacterium glutamicum and Brevibacterium lactofermentum," Appl. Microbiol. Biotechnol., 42(4):575-580 (1994)
X75504	aceA; thiX	Partial Isocitrate lyase; ?	Reinscheid, D.J. et al. "Characterization of the isocitrate lyase gene from Corynebacterium glutamicum and biochemical analysis of the enzyme," J. Bacteriol., 176(12):3474-3483 (1994)
X76875		ATPase beta-subunit	Ludwig, W. et al. "Phylogenetic relationships of bacteria based on comparative sequence analysis of elongation factor Tu and A TP-synthase beta-subunit genes," Antonie Van Leeuwenhoek, 64:285-305 (1993)
X77034	tuf	Elongation factor Tu	Ludwig, W. et al. "Phylogenetic relationships of bacteria based on comparative sequence analysis of elongation factor Tu and ATP-synthase beta-subunit genes," <i>Antonie Van Leeuwenhoek</i> , 64:285-305 (1993)
X77384	recA		Billman-Jacobe, H. "Nucleotide sequence of a recA gene from Corynebacterium glutamicum," DNA Seq., 4(6):403-404 (1994)
X78491	aceB	Malate synthase	Reinscheid, D.J. et al. "Malate synthase from Corynebacterium glutamicum pta-ack operon encoding phosphotransacetylase: sequence analysis," <i>Microbiology</i> , 140:3099-3108 (1994)
	I6S rDNA	16S ribosomal RNA	Rainey, F.A. et al. "Phylogenetic analysis of the genera Rhodococcus and Norcardia and evidence for the evolutionary origin of the genus Norcardia from within the radiation of Rhodococcus species," <i>Microbiol.</i> , 141:523-528 (1995)
	gluA; gluB; gluC; gluD	Glutamate uptake system	Kronemeyer, W. et al. "Structure of the gluABCD cluster encoding the glutamate uptake system of Corynebacterium glutamicum," J. Bacteriol., 177(5):1152-1158 (1995)
X81379	dapE	Succinyldiaminopimelate desuccinylase	Wehrmann, A. et al. "Analysis of different DNA fragments of Corynebacterium glutamicum complementing dapE of Escherichia coli," <i>Microbiology</i> , 40:3349-56 (1994)

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78200 I	16S runa	165 ribosomal KNA	Ruimy, R. et al. "Phylogeny of the genus Corynebacterium deduced from analyses of small-subunit ribosomal DNA sequences," <i>Int. J. Syst. Bacteriol.</i> , 45(4):740-746 (1995)
X82928	asd; lysC	Aspartate-semialdehyde dehydrogenase; ?	Serebrijski, I. et al. "Multicopy suppression by asd gene and osmotic stress-dependent complementation by heterologous proA in proA mutants," J. Bacteriol., 177(24):7255-7260 (1995)
X82929	proA	Gamma-glutamyl phosphate reductase	Serebrijski, I. et al. "Multicopy suppression by asd gene and osmotic stress-dependent complementation by heterologous proA in proA mutants," J. Bacteriol., 177(24):7255-7260 (1995)
X84257	16S rDNA	16S ribosomal RNA	Pascual, C. et al. "Phylogenetic analysis of the genus Corynebacterium based on 16S rRNA gene sequences," Int. J. Syst. Bacteriol., 45(4):724-728 (1995)
X85965	aroP; dapE	Aromatic amino acid permease; ?	Wehrmann et al. "Functional analysis of sequences adjacent to dapE of C. glutamicum proline reveals the presence of aroP, which encodes the aromatic amino acid transporter," J. Bacteriol., 177(20):5991-5993 (1995)
X86157	argB; argC; argD; argF; argJ	Acetylglutamate kinase; N-acetyl-gammaglutamyl-phosphate reductase; acetylornithine aminotransferase; ornithine carbamoyltransferase; glutamate Nacetyltransferase	Sakanyan, V. et al. "Genes and enzymes of the acetyl cycle of arginine biosynthesis in Corynebacterium glutamicum: enzyme evolution in the early steps of the arginine pathway," <i>Microbiology</i> , 142:99-108 (1996)
X89084	pta, ackA	Phosphate acetyltransferase; acetate kinase	Reinscheid, D.J. et al. "Cloning, sequence analysis, expression and inactivation of the Corynebacterium glutamicum pta-ack operon encoding phosphotransacetylase and acetate kinase," <i>Microbiology</i> , 145:503-513 (1999)
X89850	attB	Attachment site	Le Marrec, C. et al. "Genetic characterization of site-specific integration functions of phi AAU2 infecting "Arthrobacter aureus C70," J. Bacteriol., 178(7):1996-2004 (1996)
X90356		Promoter fragment F1	Patek, M. et al. "Promoters from Corynebacterium glutamicum: cloning, molecular analysis and search for a consensus motif," <i>Microbiology</i> , 142:1297-1309 (1996)
X90357		Promoter fragment F2	Patek, M. et al. "Promoters from Corynebacterium glutamicum: cloning, molecular analysis and search for a consensus motif," <i>Microbiology</i> , 142:1297-1309 (1996)
X90358		Promoter fragment F10	Patek, M. et al. "Promoters from Corynebacterium glutamicum: cloning, molecular analysis and search for a consensus motif," <i>Microbiology</i> , 142:1297-1309 (1996)
X90359		Promoter fragment F13	Patek, M. et al. "Promoters from Corynebacterium glutamicum: cloning, molecular analysis and search for a consensus motif," <i>Microbiology</i> , 142:1297-1309 (1996)

		Table 2 (continued)	nued)
X90360		Promoter fragment F22	Patek, M. et al. "Promoters from Corynebacterium glutamicum: cloning, molecular analysis and search for a consensus motif," <i>Microbiology</i> , 142:1297-1309 (1996)
X90361		Promoter fragment F34	Patek, M. et al. "Promoters from Corynebacterium glutamicum: cloning, molecular analysis and search for a consensus motif," <i>Microbiology</i> , 142:1297-1309 (1996)
X90362		Promoter fragment F37	Patek, M. et al. "Promoters from C. glutamicum: cloning, molecular analysis and search for a consensus motif," Microbiology, 142:1297-1309 (1996)
X90363		Promoter fragment F45	Patek, M. et al. "Promoters from Corynebacterium glutamicum: cloning, molecular analysis and search for a consensus motif," <i>Microbiology</i> , 142:1297-1309 (1996)
X90364		Promoter fragment F64	Patek, M. et al. "Promoters from Corynebacterium glutamicum: cloning, molecular analysis and search for a consensus motif," <i>Microbiology</i> , 142:1297-1309 (1996)
X90365		. Promoter fragment F75	Patek, M. et al. "Promoters from Corynebacterium glutamicum: cloning, molecular analysis and search for a consensus motif," <i>Microbiology</i> , 142:1297-1309 (1996)
X90366		Promoter fragment PF101	Patek, M. et al. "Promoters from Corynebacterium glutamicum: cloning, molecular analysis and search for a consensus motif," <i>Microbiology</i> , 142:1297-1309 (1996)
X90367		Promoter fragment PF104	Patek, M. et al. "Promoters from Corynebacterium glutamicum: cloning, molecular analysis and search for a consensus motif," <i>Microbiology</i> , 142:1297-1309 (1996)
X90368		Promoter fragment PF109	Patek, M. et al. "Promoters from Corynebacterium glutamicum: cloning, molecular analysis and search for a consensus motif," <i>Microbiology</i> , 142:1297-1309 (1996)
X93513	amt	Ammonium transport system	Siewe, R.M. et al. "Functional and genetic characterization of the (methyl) ammonium uptake carrier of Corynebacterium glutamicum," J. Biol. Chem, 271(10):5398-5403 (1996)
X93514	betP	Glycine betaine transport system	Peter, H. et al. "Isolation, characterization, and expression of the Corynebacterium glutamicum betP gene, encoding the transport system for the compatible solute glycine betaine," J. Bacteriol., 178(17):5229-5234 (1996)
X95649	orf4		Patek, M. et al. "Identification and transcriptional analysis of the dapb-ORF2-dapA-ORF4 operon of Corynebacterium glutamicum, encoding two enzymes involved in L-lysine synthesis," Biotechnol. Lett., 19:1113-1117 (1997)
X96471	lysE; lysG	Lysine exporter protein; Lysine export regulator protein	Vrljic, M. et al. "A new type of transporter with a new type of cellular function: L-lysine export from Corynebacterium glutamicum," Mol. Microbiol., 22(5):815-826 (1996)

		Table 2 (continued)	(penu
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X96580	panB; panC; xyIB	3-methyl-2-oxobutanoate hydroxymethyltransferase; pantoate-beta-alanine ligase; xylulokinase	Sahm, H. et al. "D-pantothenate synthesis in Corynebacterium glutamicum and use of panBC and genes encoding L-valine synthesis for D-pantothenate overproduction," <i>Appl. Environ. Microbiol.</i> , 65(5):1973-1979 (1999)
X96962		Insertion sequence IS1207 and transposase	
X99289		Elongation factor P	Ramos, A. et al. "Cloning, sequencing and expression of the gene encoding elongation factor P in the amino-acid producer Brevibacterium lactofermentum (Corynebacterium glutamicum ATCC 13869)," Gene, 198.217-222 (1997)
Y00140	thrB	Homoserine kinase	Mateos, L.M. et al. "Nucleotide sequence of the homoserine kinase (thrB) gene of the Brevibacterium lactofermentum," Nucleic Acids Res., 15(9):3922 (1987)
Y00151	qqp	Meso-diaminopimelate D-dehydrogenase (EC 1.4.1.16)	Ishino, S. et al. "Nucleotide sequence of the meso-diaminopimelate D-dehydrogenase gene from Corynebacterium glutamicum," Nucleic Acids Res., 15(9):3917 (1987)
Y00476	thrA	Homoserine dehydrogenase	Mateos, L.M. et al. "Nucleotide sequence of the homoserine dehydrogenase (thrA) gene of the Brevibacterium lactofermentum," <i>Nucleic Acids Res.</i> , 15(24):10598 (1987)
Y00546	hom; thrB	Homoserine dehydrogenase; homoserine kinase	Peoples, O.P. et al. "Nucleotide sequence and fine structural analysis of the Corynebacterium glutamicum hom-thrB operon," Mol. Microbiol., 2(1):63-72 (1988)
Y08964	murC; ftsQ/divD; ftsZ	UPD-N-acetylmuramate-alanine ligase; division initiation protein or cell division protein; cell division protein	Honrubia, M.P. et al. "Identification, characterization, and chromosomal organization of the ftsZ gene from Brevibacterium lactofermentum," Mol. Gen. Genet., 259(1):97-104 (1998)
Y09163	putP	High affinity proline transport system	Peter, H. et al. "Isolation of the putP gene of Corynebacterium glutamicumproline and characterization of a low-affinity uptake system for compatible solutes," Arch. Microbiol., 168(2):143-151 (1997)
Y09548	pyc	Pyruvate carboxylase	Peters-Wendisch, P.G. et al. "Pyruvate carboxylase from Corynebacterium glutamicum: characterization, expression and inactivation of the pyc gene," <i>Microbiology</i> , 144:915-927 (1998)
Y09578	leuB	3-isopropylmalate dehydrogenase	Patek, M. et al. "Analysis of the leuB gene from Corynebacterium glutamicum," Appl. Microbiol. Biotechnol., 50(1):42-47 (1998)
Y12472		Attachment site bacteriophage Phi-16	Moreau, S. et al. "Site-specific integration of corynephage Phi-16: The construction of an integration vector," Microbiol., 145:539-548 (1999)
Y12537	proP	Proline/ectoine uptake system protein	Peter, H. et al. "Corynebacterium glutamicum is equipped with four secondary carriers for compatible solutes: Identification, sequencing, and characterization of the proline/ectoine uptake system, ProP, and the ectoine/proline/glycine betaine carrier, EctP," J. Bacteriol, 180(22):6005-6012 (1998)

		Table 2 (continued)	(penu
Y13221	glnA	Glutamine synthetase I	Jakoby, M. et al. "Isolation of Corynebacterium glutamicum glnA gene encoding glutamine synthetase I," FEMS Microbiol. Lett., 154(1):81-88 (1997)
Y16642	pdį	Dihydrolipoamide dehydrogenase	
Y18059		Attachment site Corynephage 304L	Moreau, S. et al. "Analysis of the integration functions of φ304L: An integrase module among corynephages," Virology, 255(1):150-159 (1999)
Z21501	argS; lysA	Arginyl-tRNA synthetase; diaminopimelate decarboxylase (partial)	Oguiza, J.A. et al. "A gene encoding arginyl-tRNA synthetase is located in the upstream region of the lysA gene in Brevibacterium lactofermentum: Regulation of argS-lysA cluster expression by arginine," J. Bacteriol., 175(22):7356-7362 (1993)
221502	dapA; dapB	Dihydrodipicolinate synthase; dihydrodipicolinate reductase	Pisabarro, A. et al. "A cluster of three genes (dapA, orf?, and dapB) of Brevibacterium lactofermentum encodes dihydrodipicolinate reductase, and a third polypeptide of unknown function," J. Bacteriol., 175(9):2743-2749 (1993)
Z29563	thrC	Threonine synthase	Malumbres, M. et al. "Analysis and expression of the thrC gene of the encoded threonine synthase," <i>Appl. Environ. Microbiol.</i> , 60(7)2209-2219 (1994)
Z46753	16S rDNA	Gene for 16S ribosomal RNA	
249822	sigA	SigA sigma factor	Oguiza, J.A. et al "Multiple sigma factor genes in Brevibacterium lactofermentum: Characterization of sigA and sigB," J. Bacteriol., 178(2):550-553 (1996)
249823	galE; dtxR	Catalytic activity UDP-galactose 4- epimerase; diphtheria toxin regulatory protein	Oguiza, J.A. et al "The galE gene encoding the UDP-galactose 4-epimerase of Brevibacterium lactofermentum is coupled transcriptionally to the dmdR gene," Gene, 177:103-107 (1996)
249824	orfl; sigB	?; SigB sigma factor	Oguiza, J.A. et al "Multiple sigma factor genes in Brevibacterium lactofermentum: Characterization of sigA and sigB," J. Bacteriol., 178(2):550-553 (1996)
266534		Transposase	Correia, A. et al. "Cloning and characterization of an IS-like element present in the genome of Brevibacterium lactofermentum ATCC 13869," <i>Gene</i> , 170(1):91-94 (1996)
' A sequence for the published ver	this gene was published in sion. It is believed that the	the indicated reference. However, the sequence published version relied on an incorrect start c	A sequence for this gene was published in the indicated reference. However, the sequence obtained by the inventors of the present application is significantly longer than the published version. It is believed that the published version relied on an incorrect start codon, and thus represents only a fragment of the actual coding region.

TABLE 3: Corynebacterium and Brevibacterium Strains Which May be Used in the Practice of the Invention

Genus = 🚎	species : 3	ATCC	FERM	NRRL	CEGT	NGIMB	EBS#	NCTE	DSMZ
Brevibacterium	ammoniagenes	21054							
Brevibacterium	ammoniagenes	19350							<u> </u>
Brevibacterium	ammoniagenes	19351							
Brevibacterium	ammoniagenes	19352							
Brevibacterium	ammoniagenes	19353							
Brevibacterium	ammoniagenes	19354							
Brevibacterium	ammoniagenes	19355			i – –				
Brevibacterium	ammoniagenes	19356	1						
Brevibacterium	ammoniagenes	21055							
Brevibacterium	ammoniagenes	21077							
Brevibacterium	ammoniagenes	21553							
Brevibacterium	ammoniagenes	21580							
Brevibacterium	ammoniagenes	39101							
Brevibacterium	butanicum	21196							
Brevibacterium	divaricatum	21792	P928						
Brevibacterium	flavum	21474							
Brevibacterium	flavum	21129							
Brevibacterium	flavum	21518						,	
Brevibacterium	flavum			B11474					
Brevibacterium	flavum			B11472					
Brevibacterium	flavum	21127							
Brevibacterium	flavum	21128							
Brevibacterium	flavum	21427							
Brevibacterium	flavum	21475							
Brevibacterium	flavum	21517							
Brevibacterium	flavum	21528							
Brevibacterium	flavum	21529							
Brevibacterium	flavum			B11477					
Brevibacterium	flavum			B11478					
Brevibacterium	flavum	21127							
Brevibacterium	flavum			B11474					
Brevibacterium	healii	15527							
Brevibacterium	ketoglutamicum	21004							
Brevibacterium	ketoglutamicum	21089							
Brevibacterium	ketosoreductum	21914							
Brevibacterium	lactofermentum				70				
Brevibacterium	lactofermentum				74				
Brevibacterium	lactofermentum				77				
Brevibacterium	lactofermentum	21798							
Brevibacterium	lactofermentum	21799							
Brevibacterium	lactofermentum	21800							
Brevibacterium	lactofermentum	21801							
Brevibacterium	lactofermentum			B11470					
Brevibacterium	lactofermentum			B11471					

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Genus 200	species@on # 10	ATCC **	EERM	ENRRITE	CEGE	NCIMB	* CBS	NCTG	DSMZ
Brevibacterium	lactofermentum	21086		THE PERSON	\$7.79(33.70°	Spring to the second	TO SUBSECULAR	1000	<u> 17 14 200</u>
Brevibacterium	lactofermentum	21420			<u> </u>		ļ- 	 -	
Brevibacterium	lactofermentum	21086	ļ		<u> </u>				
Brevibacterium	lactofermentum	31269							
Brevibacterium	linens	9174							
Brevibacterium	linens	19391			<u> </u>				
Brevibacterium	linens	8377							
Brevibacterium	paraffinolyticum				 	11160			
Brevibacterium	spec.			-		17700	717.73		
Brevibacterium	spec.				 		717.73		
Brevibacterium	spec.	14604			 				
Brevibacterium	spec.	21860			-				
Brevibacterium	spec.	21864							
Brevibacterium	spec.	21865	-						
Brevibacterium	spec.	21866							
Brevibacterium	spec.	19240				-			
Corynebacterium	acetoacidophilum	21476			\vdash				
Corynebacterium	acetoacidophilum	13870							
Corynebacterium	acetoglutamicum			B11473					
Corynebacterium	acetoglutamicum			B11475					
Corynebacterium	acetoglutamicum	15806							
Corynebacterium	acetoglutamicum	21491							
Corynebacterium	acetoglutamicum	31270							
Corynebacterium	acetophilum			B3671					
Corynebacterium	ammoniagenes	6872						2399	
	ammoniagenes	15511							
_	fujiokense	21496							
Corynebacterium	glutamicum	14067					_		
Corynebacterium	glutamicum	39137							
Corynebacterium	glutamicum	21254							
Corynebacterium	glutamicum	21255							
Corynebacterium	glutamicum	31830							
Corynebacterium	glutamicum	13032							
Corynebacterium	glutamicum	14305							
Corynebacterium	glutamicum	15455							
Corynebacterium	glutamicum	13058							
Corynebacterium	glutamicum	13059							
Corynebacterium	glutamicum	13060							
Corynebacterium	glutamicum	21492							
Corynebacterium	glutamicum	21513							
Corynebacterium	glutamicum	21526							
Corynebacterium	glutamicum	21543	·-··						
Corynebacterium	glutamicum	13287			_				
Corynebacterium	glutamicum	21851							
Corynebacterium	glutamicum	21253							
Corynebacterium	glutamicum	21514							
Corynebacterium	glutamicum	21516							
Corynebacterium	glutamicum	21299							

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Genust量 建氯甲酚	species et la	ATCC	FERM	NRRL	CEGT	NEIMB	變GBS型	NCTE	DSMZ
Corynebacterium	glutamicum	21300	water and the part of the part of	and the second	20 0 m 980 6	and rapid forthering	Applicated a second	nungan neuthir (se Tel	AND DESCRIPTION OF THE
Corynebacterium	glutamicum	39684	<u> </u>	<u> </u>					
Corynebacterium	glutamicum	21488			 				
Corynebacterium	glutamicum	21649							
Corynebacterium	glutamicum	21650						-	
Corynebacterium	glutamicum	19223							
Corynebacterium	glutamicum	13869							
Corynebacterium	glutamicum	21157							
Corynebacterium	glutamicum	21158			·				
Corynebacterium	glutamicum	21159							
Corynebacterium	glutamicum	21355							
Corynebacterium	glutamicum	31808							
Corynebacterium	glutamicum	21674							
Corynebacterium	glutamicum	21562							
Corynebacterium	glutamicum	21563				-			
Corynebacterium	glutamicum	21564			ļ				
Corynebacterium	glutamicum	21565							
Corynebacterium	glutamicum	21566							
Corynebacterium	glutamicum	21567							
Corynebacterium	glutamicum	21568							
Corynebacterium	glutamicum	21569							
Corynebacterium	glutamicum	21570							
Corynebacterium	glutamicum	21571							
Corynebacterium	glutamicum	21572							
Corynebacterium	glutamicum	21573							
Corynebacterium	glutamicum	21579	•						
Corynebacterium	glutamicum	19049	,						V
Corynebacterium	glutamicum	19050							
Corynebacterium	glutamicum	19051							
Corynebacterium	glutamicum	19052							
Corynebacterium	glutamicum	19053							
Corynebacterium	glutamicum	19054							
Corynebacterium	glutamicum	19055					·		
	glutamicum	19056							
	glutamicum	19057							
	glutamicum	19058							
	glutamicum	19059							
Corynebacterium	glutamicum	19060							
	glutamicum	19185							
	glutamicum	13286							
	glutamicum	21515							
	glutamicum	21527							
	glutamicum	21544							
	glutamicum	21492							
	glutamicum			B8183					
	glutamicum			B8182					
	glutamicum			B12416					
Corynebacterium	glutamicum			B12417					

Genus : 12 # # ¥ # M	species 生生素素	写ATCC製	FERM	NRRL	CECT	NGIMB	* CBS	NCTE	DSMZ'
Corynebacterium	glutamicum			B12418					
Corynebacterium	glutamicum			B11476					
Corynebacterium	glutamicum	21608							
Corynebacterium	lilium		P973						
Corynebacterium	nitrilophilus	21419				11594			
Corynebacterium	spec.		P4445						
Corynebacterium	spec.		P4446						
Corynebacterium	spec.	31088							
Corynebacterium	spec.	31089						<u> </u>	
Corynebacterium	spec.	31090							
Corynebacterium	spec.	31090							
Corynebacterium	spec.	31090							
Corynebacterium	spec.	15954							20145
Corynebacterium	spec.	21857							
Corynebacterium	spec.	21862							
Corynebacterium	spec.	21863							

ATCC: American Type Culture Collection, Rockville, MD, USA

FERM: Fermentation Research Institute, Chiba, Japan

NRRL: ARS Culture Collection, Northern Regional Research Laboratory, Peoria, IL, USA

CECT: Coleccion Espanola de Cultivos Tipo, Valencia, Spain

NCIMB: National Collection of Industrial and Marine Bacteria Ltd., Aberdeen, UK

CBS: Centraalbureau voor Schimmelcultures, Baarn, NL

NCTC: National Collection of Type Cultures, London, UK

DSMZ: Deutsche Sammlung von Mikroorganismen und Zellkulturen, Braunschweig, Germany

For reference see Sugawara, H. et al. (1993) World directory of collections of cultures of microorganisms: Bacteria, fungi and yeasts (4th edn), World federation for culture collections world data center on microorganisms, Saimata, Japen.

TABLE 4: ALIGNMENT RESULTS Source of Genbank Hit % homology. Date of Genbank Hit % homology.	mo sapiens clone NH0501G22, *** SEQUENCING IN PROGRESS ***, 3 Homo sapiens 39,080 5-Jun-99 ordered pieces.	39,264 36,725	Homo sapiens CAGH44 mRNA, partial cds. Homo sapiens 38,957 18-DEC-1997 HS_2245_A1_F07_MF CIT Approved Human Genomic Sperm Library D Homo Homo sapiens 45,066 16-OCT-1998	sapiens genorific done frage 2243 Cut- 13 now- 1, genorific suivey sequence. Drosophila melanogaster chromosome 2 clone BACR45O18 (D527) RPCI-98 45.01 and a strain y; cn bw sp, *** SEQUENCING IN PROGRESS***, a by sp, *** SEQUENCING IN PROGRESS**	Drosophila melanogaster chromosome 2 clone BACR45O18 (D527) RPCI-98 Drosophila melanogaster 36,589 13-OCT-1999 45.O.18 map 41E-41E strain y; cn bw sp, *** SEQUENCING IN PROGRESS***, 13 unordered pieces.	Streptomyces coelicolor cosmid 9C7. Streptomyces coelicolor cosmid 9C7. Streptomyces coelicolor cosmid 9C7. Streptomyces coelicolor cosmid 9C7. Streptomyces coelicolor 36,313 12-Apr-99 1 Streptomyces coelicolor 36,313 12-Apr-99 1 Streptomyces coelicolor 36,313 12-Apr-99 1 Burkholderia pseudomallei strain 1026b DbhB (dbhB), general secretory pathway protein E (gspE), general secretory pathway protein H (gspC), general secretory pathway protein L (gspL), general secretory pathway protein N (gspM), and general secretory pathway protein N	(gspN) genes, complete cds; and unknown genes. za65g02.s1 Soares fetal liver spleen 1NFLS Homo sapiens CDNA clone Homo sapiens 40,420 29-MAR-1996 IMAACE::202458 31 MBNA sequence	SHGC-56832 Human Homo sapiens STS genomic, sequence tagged site. Homo sapiens 40,420 30-MAR-1998	SHGC-56832 Human Homo sapiens STS genomic, sequence tagged site. Homo sapiens 40,420 30-MAR-1998	cobacterium tuberculosis H37Rv complete genome; segment 133/162. Mycobacterium 60,271 17-Jun-98 tuberculosis	Escherichia coli genomic sequence of minutes 9 to 12. Escherichia coli K-12 MG1655 section 55 of 400 of the complete genome. Escherichia coli K-12 MG1655 section 55 of 400 of the complete genome.	Streptomyces coelicolor A3(2)	Drosophila melanogaster genome survey sequence SP6 end of BAC BACN14G08 Drosophila melanogaster 37,573 26-Jul-99
TAB	£Š	Homo sapiens B.nigra DNA fo	Homo sapiens of HS_2245_A1_F	2 5 5 5	2 45 CT		(gspN) genes, complete cds; and uni za65g02.s1 Soares fetal liver spleen	SHGC-56832 P	SHGC-56832 H	Mycobacterium			
Accession	185001 AC007366	U80741 X89901	U80741 AQ163721	171979 AC007054	171979 AC007054	AL035161 AL049628 AF110185	N80167	G37084	G37084	Z83866	U82598 AE000165	AL096837	AL105910
Length		912	912 388			31360 38532 20302	384	38 4	384	31859	136742 12003	35437	1036
length Genbank Hit (NT)	GB_HTG2:AC007366	GB_PR3:HSU80741 912 GB_PL1:BNDNATRNA 1732	GB_PR3:HSU80741 GB_GSS9:AQ163721	GB_HTG4:AC007054	GB_HTG4:AC007054	GB_BA1:SC9C7 GB_BA1:SCE94 GB_BA2:AF110185	GB_EST6:N80167	GB_STS:G37084	GB_STS:G37084	GB_BA1:MTCY22D7	GB_BA1:ECU82598 GB_BA2:AE000165	GB_BA1:SCF43A	GB_GSS2:CNS015U4 1036
ID# length (NT)	rxa00062 1521	ra00084 948	rxa00109 735			rxa00215 1449	rxa00289 1299			rxa00404 2439		rxa00479 2313	

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				Table 4 (continued)			
rxa00810 324	GB_BA1:MTY15C10	33050	Z95436	Mycobacterium tuberculosis H37Rv complete genome; segment 154/162.	Mycobacterium tuberculosis	34,615	17-Jun-98
	GB_BA1:MLCB2548	38916	-	Mycobacterium leprae cosmid B2548.	Mycobacterium leprae	34,615	27-Aug-99
	GB_BA1:ECOUW76	225419		E. coli chromosomal region from 76.0 to 81.5 minutes.	Escherichia coli	52,997	7-Nov-96
rxa00829 2463	GB_BA1:SC5C7	41906	AL031515	Streptomyces coelicolor cosmid 5C7.	Streptomyces coelicolor	65,269	7-Sep-98
	GB_BA1:SC5F2A	40105	AL049587	Streptomyces coelicolor cosmid 5F2A.	Streptomyces coelicolor	37,490	24-MAY-1999
	GB_BA1:STMDRRC	3374	L76359	Streptomyces peucetius daunorubicin resistance protein (drrC) gene, complete	Streptomyces peucetius	55,279	24-DEC-1996
rxa00843 468	GB_BA1:MTCY9C4	15916	277250	Mycobacterium tuberculosis H37Rv complete genome; segment 113/162.	Mycobacterium tuberculosis	40,000	17-Jun-98
	GB_BA1:MTCY9C4	15916	277250	Mycobacterium tuberculosis H37Rv complete genome; segment 113/162.	Mycobacterium tuberculosis	37,773	17-Jun-98
rxa00858 568	GB_BA1:SCC54	30753	AL035591	Streptomyces coelicolor cosmid C54.	Streptomyces coelicolor	39,602	11-Jun-99
	GB_EST18:N96610	547	N96610	21285 Lambda-PRL1 Arabidopsis thaliana cDNA clone F10G3T7, mRNA	Arabidopsis thaliana	37,801	5-Jan-98
	GB_EST18.T45493	436		8756 Lambda-PRL2 Arabidopsis thaliana cDNA clone 133C14T7, mRNA	Arabidopsis thaliana	34,194	4-Aug-98
rxa00886 1269	GB_BA1:SYCSLLLH	132106		Synechocystis sp. PCC6803 complete genome, 25/27, 3138604-3270709.	Synechocystis sp.	37,459	13-Feb-99
	GB_BA1:SCDNAJ	5611	X77458	S.coelicolor dnaK, grpE and dnaJ genes.	Streptomyces coelicolor	49,744	21-Nov-96
	GB_BA1:STMDNAK	4648	L46700	Streptomyces coelicolor (strain A3(2)) dnaK operon encoding molecular	Streptomyces coelicolor	49,583	22-Nov-96
				chaperones (dnaK, dnaJ), gmE and hspR genes, complete cds's.			_
rxa00900 975	GB_BA2:ECOUW67_0 110000	110000		Escherichia coli K-12 chromosomal region from 67.4 to 76.0 minutes.	Escherichia cofi	38,314	U18997 08
	GB_BA2:ECOUW67_0 110000	110000		Escherichia coli K-12 chromosomal region from 67.4 to 76.0 minutes.	Escherichia coli	37,759	U18997 I
	GB_BA2:AE000393	10516		Escherichia coli K-12 MG1655 section 283 of 400 of the complete genome.	Escherichia coli	38,314	12-Nov-98
xa00901 537	GB_HTG3:AC010757	175571	AC010757	Homo sapiens chromosome 18 clone 128_C_18 map 18, *** SEQUENCING IN	Homo sapiens	34,857	22-Sep-99
	CB UTC3-AC010757	175571	175571 0000057	PROGRESS ***, 20 unordered pieces.			
	7670100X-201013V	1.00.1	¥001004	PROGRESS ***, 20 unordered pieces.	nomo sapiens	34,857	22-Sep-99
	GB_HTG3:AC011283	87295	AC011283	Homo sapiens clone MS2016A09, *** SEQUENCING IN PROGRESS ***, 1	Homo sapiens	35,448	07-OCT-1999
				unordered pieces.			
rxa00981 753	GB_OV:GGA245664	512	AJ245664	Gallus gallus partial mRNA for ATP-citrate lyase (ACL gene).	Gallus gallus	37,538	28-Sep-99
	GB_PL2:AC007887	159434	159434 AC007887	Genomic sequence for Arabidopsis thaliana BAC F1504 from chromosome I,	Arabidopsis thaliana	37,600	04-OCT-1999
	GB_GSS1:CNS00RNW542	V542	AL087338	Soliptice sequence. Arabidopsis thaliana genome survey sequence T7 end of BAC F14D7 of IGF	Arabidopsis thaliana	41,264	28-Jun-99
				library from strain Columbia of Arabidopsis thaliana, genomic survey sequence.	-		
rxa00995 864	GB_EST29:A1553951	450	AI553951	te54d01.x1 Soares_NFL_T_GBC_S1 Homo sapiens cDNA clone IMAGE:2090497 Homo sapiens 3' similar to gb:X02067 H.sapiens mRNA for 7SL RNA pseudogene (HUMAN);, mRNA sequence	Homo sapiens	42,627	13-Apr-99
	GB_PR3:AC003029	139166	139166 AC003029	Homo sapiens Chromosome 12q24 PAC RPCI3-462E2 (Roswell Park Cancer	Homo sapiens	38,915	17-Sep-98
	1	,		Institute Human PAC library) complete sequence.			
# 00 0000 or 11	GB_BAT:EAY14603		Y146U3	Erwinia amylovora srlA, srlE, srlB, srlD, srlM and srlR genes.	Erwinia amylovora	37,694	6-Jan-98
14400330 004	GB_EST30:AV018764	26,50	AV018764	AV019764 Mus musculus section 105 of 172 of the complete genome.	Archaeoglobus fulgidus	41,078	15-DEC-1997
				1190006M16, mRNA sequence.	ivius muscalus	600'60	66-6nV-07

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10-OCT-1997	12-Jul-97 19-DEC-1996	12-Sep-96	21-MAY-1999	04-DEC-1999	19-Jul-99	2-Aug-97 2-Aug-97	7-Feb-99	07-DEC-1999	07-DEC-1999	10-Feb-99	03-DEC-1999	03-DEC-1999	08-OCT-1999	08-OCT-1999 10-lun-94		21-Apr-98 19-Aug-99	19-Aug-99	14-Aug-98 14-Aug-98 AC011500	23-Sep-99
44 385	46,629 38,677	58,696	37,651	36,011	38,640	39,344 38,780	39,205	32,961	38,476	42,925	36,825	36,825	35,794	40,625 37,793	} <u>-</u>	35,014 17,697	17,697	38,195 36,611 36,446	35,764
Arabidonsis thaliana	Coturnix coturnix Mus musculus	Mus musculus	Homo sapiens	s Homo sapiens	Homo sapiens	Caenorhabditis elegans Caenorhabditis elegans	Gallus gallus	Homo sapiens	Homo sapiens	Ipomoea nil	Homo sapiens	Homo sapiens	Caenorhabditis elegans	Caenorhabditis elegans Mus musculus		Neisseria meningitidis Plasmodium falciparum	Plasmodium falciparum	Homo sapiens Homo sapiens Homo sapiens	Homo sapiens
Table 4 (continued) F19F16TF IGF Arabidonsis thaliana genomic close F19F16 genomic survey	sequence. Coturnix coturnix arylalkylamine N-acetyltransferase mRNA, partial cds. ms50c09.rt Life Tech mouse embryo 13 5dpc 10666014 Mus musculus cDNA	cione IMAGE:014992.5 similar to SW:NEST_RAT_P21253 NESTIN.;, mRNA sequence. mrs. sequence. mrs. mrs. mrs. mrs. mrs. mrs. mrs. mrs	sequence. RPCI11-135F10.TJ RPCI-11 Homo sapiens genomic clone RPCI-11-135F10,	genomic survey sequence. Home sapiens clone RP11-544J22, WORKING DRAFT SEQUENCE, 1 unordered Home sapiens	pieces. HS_5538_A1_A11_T7A RPCI-11 Human Male BAC Library Homo sapiens	genomic done Prace=1114 Col=21 Kow=A, genomic survey sequence. Caenorhabditis elegans cosmid C13D9. Caenorhabditis elegans cosmid C13D9.	Chicken novel maf-related gene mafG encoding bZip nuclear protein MafG,	promoter region and exon 1. Homo sapiens clone RP11-115N6, *** SEQUENCING IN PROGRESS ***, 26	unordered pieces. Homo sapiens clone RP11-115N6, *** SEQUENCING IN PROGRESS ***, 26	unordered pieces. Pharbitis nil mRNA for Pharbitis nil Germin-like protein precursor, complete cds.	Homo sapiens chromosome 6 clone RP3-402N21 map p21.1-21.31,	Homo sapiens chromosome 6 clone RP3-402N21 map p21.1-21.31, ****SEQUENCING IN PROGRESS ***, in unordered pieces.	Caenorhabditis elegans cosmid F18A12.	Caenorhabditis elegans cosmid F18A12. Mouse cystic fibrosis transmembrane conductance regulator (CFTR) mRNA.	complete cds.	Neisseria meningitidis chloramphenicol acetyltransferase gene, complete cds. Plasmodium falciparum chromosome 13 strain 3D7, *** SEQUENCING IN PROGRESS *** in unordered pieces.	Plasmodium falciparum chromosome 13 strain 3D7, *** SEQUENCING IN PROGRESS *** in unordered nieces	Homo sapiens chromosome 17, clone hRPK.214_O_1, complete sequence. Homo sapiens chromosome 17, clone hRPK.214_O_1, complete sequence. Homo sapiens chromosome 19 clone CIT978SKB_60E11, *** SEQUENCING IN	PROGRESS ***, 246 unordered pieces. Homo sapiens clone 6_L_24, LOW-PASS SEQUENCE SAMPLING.
B24189	AF007068 AA166324	W89968	AQ381423	206121 AC010901	AQ746932	AF016420 AF016420	D28601	AC010765	146468 AC010765	D45425	AL049553	AL049553	AF016688	AF016688 M60493		AF031037 AL109815	AL109815	AC005224 AC005224 AC011500	AC010831
377		46	579	206121	837	43487 43487	1316	146468	146468	962	1/0302	170302	29784	29784 6304		1472 480518	A80518	166687 166687 1300851	70233
GB GSS3:B24189	GB_EST10:AA166324	GB_EST7:W89968	GB_GSS12:AQ381423 579	GB_HTG6:AC010901	GB_GSS5:AQ746932	GB_IN1:CELC13D9 GB_IN1:CELC13D9	GB_OV:CHKMAFG1	GB_HTG6:AC010765 146468 AC010765	GB_HTG6:AC010765	GB_PL1:PHNPNGLP	GB_HIGZ:HSJ4UZNZ1 1/030Z ALU49553	GB_HTG2:HSJ402N21 170302	GB_IN2:CELF18A12	GB_INZ:CELF18A12 GB_RO:MUSMCFTR		GB_BA2:AF031037 1472 GB_HTG1:PFMAL13PA80518	GB_HTG1:PFMAL13PA80518	GB_PR3:AC005224 166687 GB_PR3:AC005224 166687 GB_HTG3:AC011500_1300851	GB_HTG3:AC010831
	rxa01010 1242		rxa01051 732			xa01052 432	rxa01053 543			rxa01054 612			xa01217 723			rxa01320 1770		ra01345 1575	rxa01407 1014

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23-Sep-99 30-Sep-98 1-Aug-99 3-Sep-99	3-Sep-99 26-Nov-97 2-Aug-99	2-Aug-99 14-Jul-99 14-Jul-99 23-Sep-97	0 0 10-Sep-99 1 23-Nov-98 21-DEC-1998 9-Apr-97	23-Aug-99 23-Aug-99 01-MAY-1999	13-Jul-99 04-OCT-1999 22-Aug-99 22-Aug-99 8-Sep-99 26-Apr-93
35,764 40,778 41,234 er 39,432	ar 39,432 38,201 ar 38,302	38,302 37,873 40,220 42,960	37,626 37,237 38,406 99,933	er 36,111 er 36,111 39,537	36,419 36,317 35,303 35,409 35,409
Homo sapiens 35,764 Homo sapiens 40,778 Homo sapiens 41,234 Drosophila melanogaster 39,432	Drosophila melanogaster 39,432 Bacillus subtilis 38,201 Drosophila melanogaster 38,302	Drosophila melanogaster 38,302 Homo sapiens 37,873 Homo sapiens 40,220 Raistonia eutropha 42,960	Vogesella indigofera Caenorhabditis elegans Homo sapiens Corynebacterium	Drosophila melanogaster 36,111 Drosophila melanogaster 36,111 Daucus carota 39,537	Homo sapiens Homo sapiens Homo sapiens Homo sapiens Escherichia coli
Table 4 (continued) Homo sapiens clone 6_L_24, LOW-PASS SEQUENCE SAMPLING. Homo sapiens chromosome 4 clone B241P19 map 4q25, complete sequence. Homo sapiens constitutive fragile region FRA3B sequence. Drosophila melanogaster chromosome 3 clone BACR02G21 (D722) RPCI-98 02.G.21 map 90E-91A strain y; cn bw sp, *** SEQUENCING IN PROGRESS***, 89 unordered blaces.	ister chromosome 3 clone BACR02G21 (D722) RPCI-98 A strain y; cn bw sp, *** SEQUENCING IN PROGRESS***, oldete genome (section 15 of 21); from 2785131 to 3013540. Ister chromosome 2 clone BACR13J10 (D924) RPCI-98 Strain y; cn bw sp, *** SEQUENCING IN PROGRESS***,	Drosophila melanogaster chromosome 2 clone BACR13J10 (D924) RPCI-98 13.J.10 map 47B 47C strain y; cn bw sp, *** SEQUENCING IN PROGRESS ***, 82 unordered pieces. Homo sapiens 14q32 Jagged2 gene, complete cds; and unknown gene. Homo sapiens 14q32 Jagged2 gene, complete cds; and unknown gene. Alcaligenes eutrophus genes for ureases, ureD1, ureD2, ureA, ureB, and ORF1,	ORF2. Vogesella indigofera indigoidine biosynthesis regulatory locus, complete Caenorhabditis elegans cosmid M04D8, complete sequence. qt82d04.x1 NCI_CGAP_Co14 Homo sapiens cDNA clone IMAGE:1961767 3', mRNA sequence. Corynebacterium glutamicum multidrug resistance protein (cmr) gene, complete cds.	Drosophila melanogaster chromosome 3 clone BACR09F18 (D812) RPCI-98 09.F.18 map 98D-98D strain y; cn bw sp, *** SEQUENCING IN PROGRESS ***, 109 unordered pieces. Drosophila melanogaster chromosome 3 clone BACR09F18 (D812) RPCI-98 09.F.18 map 98D-98D strain y; cn bw sp, *** SEQUENCING IN PROGRESS***, 109 unordered pieces. Daucus carota mRNA for citrate synthase, complete cds.	Homo sapiens endothelial nitric oxide synthase gene, complete cds. Homo sapiens clone NH0166D23, *** SEQUENCING IN PROGRESS ***, 7 unordered pieces. Homo sapiens chromosome 9 clone 30_C_23 map 9, *** SEQUENCING IN PROGRESS ***, 20 unordered pieces. Homo sapiens chromosome 9 clone 30_C_23 map 9, *** SEQUENCING IN PROGRESS ***, 20 unordered pieces. Homo sapiens clone 115_I_23, LOW-PASS SEQUENCE SAMPLING. E.coli protein p7 (neu C) gene, complete cds.
AC010831 AC004058 AF152365 AC007890	121256 AC007890 218410 Z99118 107439 AC008260	107439 AC008260 148083 AF111170 148083 AF111170 6740 Y13732	AF088857 Z32682 AI281910 U43535	114735 AC009213 114735 AC009213 1859 AB017159	154754 AC011234 124337 AC009450 124337 AC009450 134724 AC009919 1676 M84026
70233 38400 246546 121256	121256 218410 107439	107439 148083 1740 6740	2908 21552 276 2531	114735	154754 154754 124337 134724 1676
GB_HTG3:AC010831 GB_PR3:AC004058 GB_PR4:AF152365 GB_HTG3:AC007890	GB_HTG3:AC007890 GB_BA1:BSUB0015 GB_HTG2:AC008260	GB_HTG2:AC008260 107439 AC008260 GB_PR4:AF111170 148083 AF111170 GB_PR4:AF111170 148083 AF111170 GB_BA1:AEY13732 6740 Y13732	GB_BA2:AF088857 GB_IN1:CEM04D8 GB_EST25:AI281910 GB_BA1:CGU43535	GB_HTG3:AC009213 114735 AC009213 GB_HTG3:AC009213 114735 AC009213 GB_PL1:AB017159 1859 AB017159	GB_HTG3:AC011234 154754 AC011234 GB_HTG3:AC0011234 154754 AC011234 GB_HTG3:AC009450 124337 AC009450 GB_HTG3:AC009950 124337 AC009950 GB_HTG3:AC009919 134724 AC009919 GB_BA1:ECONEUC 1676 M84026
rxa01408 324	rxa01524 1566	ra01578 1510	ra01616 1605	rxa01674 1017	rxa01873 1359

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	2-Aug-99	2-Aug-99	16-OCT-1999	16-OCT-1999	26-Nov-98	18-OCT-1995	6-Jul-94	16-Jul-96			25-Sep-98	3661-NAM-+7	27-Aug-99	3-Aug-99	3-Aug-99	3-Aug-99	1-, lut-98				5-Jan-99	;	5-Jan-99	24-Jun-98	21-Jul-99	
	er 34,365	er 34,365	er 38,534	er 38,534	36,249	45,679	36,232	42,969			35,724	080'66	38,128	36,662	36,662	34,768	99 843				88,679		100,000	38,951	36,774	
	Drosophila melanogaster 34,365 0	Drosophila melanogaster 34,365	Drosophila melanogaster 38,534	Drosophila melanogaster	Homo sapiens	Homo sapiens	Saccharopolyspora exthraea	Mus musculus			Homo sapiens Arabidoneis thalians	Alabidopolo illanaria	Arabidopsis thaliana	Homo sapiens	Homo sapiens	Homo sapiens	Corvnebacterium	e glutamicum			Corynebacterium	glutamicum	Corynebacterium	Bacillus subtilis	Danio rerio	
Table 4 (continued)	Drosophila melanogaster chromosome 3 clone BACR03L02 (D766) RPCI-98 03.L.2 map 96B-96C strain y; cn bw sp, *** SEQUENCING IN PROGRESS ***, 80 unordered pieces.	Drosophila melanogaster chromosome 3 clone BACR03L02 (D766) RPCI-98 03.L.2 map 96B-96C strain y; cn bw sp, *** SEQUENCING IN PROGRESS***, 80 unordered pieces.	Drosophila melanogaster chromosome 3L/66B6 clone RPC198-6E4, *** SEQUENCING IN PROGRESS ***, 52 unordered pieces.	Drosophila melanogaster chromosome 3L/6686 clone RPCI98-6E4, *** SEQUENCING IN PROGRESS ***, 52 unordered piaces.	Homo sapiens chromosome 17, clone hRPK.212_E_8, complete sequence.	H.Sapiens CpG island DNA genomic Mse1 fragment, clone 169c8, forward read cpg169c8.ft1a.	Saccharopolyspora erythraea excisionase (xis) gene, integrase (int) gene, complete cds's and attB site.	mf98a09.r1 Soares mouse embryo NbME13.5 14.5 Mus musculus cDNA clone IMAGE:422296 5' mRNA sequence			Homo sapiens chromosome 17, clone hRPK.349_A_8, complete sequence. Arabidoosis thaliana DNA chromosome 4_BAC clone_F20R18 (FSSA project)	בייניסיסיסיס היינייים כולא כוויסיסיסיופין, סאט המוופי בסבוים (בסכא ףוטפען).	Arabidopsis thaliana DNA chromosome 4, BAC clone (ESSA project).	Homo sapiens chromosome 5 clone CIT978SKB_70D3, *** SEQUENCING IN PROGRESS ***, 54 unordered pieces.	Homo sapiens chromosome 5 clone CIT978SKB_70D3, *** SEQUENCING IN PROGRESS *** 54 unordered pieces.	Homo sapiens chromosome 5 clone CIT978SKB_76P12, *** SEQUENCING IN	r NOGRESS 1, 34 unoldered pieces. Corynebacterium glutamicum N-acetylglutamylphosphate reductase (araC).	ornithine acetyltransferase (arg.), N-acetylglutamate kinase (arg.B.), acetylornithine glutamicum	(argR), argininosuccinate synthase (argG), and argininosuccinate Iyase (argH)	genes, complete cds.	Corynebacterium glutamicum ornithine carbamolytransferase (argF) gene,	complete cds.	Corynebacterium giutamicum arginine repressor (argix) gene, complete cds.	B.sublilis yws[A,B,C] genes and rbs[A,C,D,K,R] genes.	fc57a12.y1 Zebrafish WashU MPIMG EST Danio rerio cDNA 5' similar to	IN. RISTST RISTST RETEROGENEDOS NOCLEAR RIBONOCLEOPROTEIN AU .; MRNA sequence.
	AC007853	AC007853	166249 AC010037	166249 AC010037	167228 AC005552	6 57,539	L11597	W97557			169045 AC005544 104738 AL049483		AL049171	AC008697	167932 AC008697	213971 AC008703	AF049897				AF031518	0044436	7104:430	Z92953	A1878071	
	116280	116280	166249	166249	167228	243		267			169045		89904	16/932	167932	213971	9196				2045	212		**	293	
	GB_HTG2:AC007853 116280 AC007853	GB_HTG2:AC007853 116280 AC007853	GB_HTG4:AC010037	GB_HTG4:AC010037	GB_PR4:AC005552	GB_PK1:HS109C8F	GB_BA1:SERATTBXIS 3255	GB_EST7:W97557			GB_PR3:AC005544 GB_PL1:ATF20B18		GB_PL2:ATT25K17	GB_H1G3:AC008697	GB_HTG3:AC008697	GB_HTG3:AC008703	GB_BA2:AF049897				GB_BA2:AF031518	CB BA2.AE041436	00717017070	GB_BA1:BSZ92953	GB_EST36:AI878071	
			rxa01936 1395		000000	1x801964 420			xa02060		rxa02087 1470		00000	rxauzu88 1338			rxa02159 636							rxa02184 504		

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20-Aug-99	23-Nov-99	28-Jul-99	28-Jul-99	29-Jun-95	29-Jun-95	08-DEC-1995	86-UDC-67	66-Jnr-82		84 8Nov-11		10-Feb-99	13-Jan-95	27-Aug-99 2-Anr-98		23-Nov-99	23-Nov-99	19-MAY-1998	28-DEC-1995		28-DEC-1995	17-Jan-98	06-MAY-1999	20-Aug-99
36,774	38,648	35,938	35,938	38,267	36,552		0 0	35,568	40,310	40,310	37,703	38,420	42,188	42,000 39,098		39,456	39,456	is 49,369	35,417		37,172	42,115	52,059	45,438
Danio rerio	Homo sapiens	Mus musculus	Mus musculus	', Homo sapiens	, Homo sapiens	Caenorhabditis elegans		nomo sapiens	Homo sapiens	Homo sapiens	Brugia pahangi	Mus musculus	Homo sapiens	Mycobacterium leprae Rattus sp.		Homo sapiens	Homo sapiens	Xanthomonas campestris 49,369	Homo sapiens		Homo sapiens	Deinococcus	proteolyticus Danio rerio	Danio rerio
fc91f01.y1 Zebrafish WashU MPIMG EST Danio rerio cDNA 5' similar to TR:Q13151 Q13151 HETEROGENEOUS NUCLEAR RIBONUCLEOPROTEIN A0	., includes sequence. Human DNA sequence from clone 494O16 on chromosome 22, complete sequence.	Sequence. Mus musculus clone 182_H_5, *** SEQUENCING IN PROGRESS ***, 29	unordered pieces. Mus musculus clone 182_H_5, *** SEQUENCING IN PROGRESS ***, 29	unordered pieces. ym34a11.r1 Soares infant brain 1NIB Homo sapiens cDNA clone IMAGE:50010 5', Homo sapiens	mRNA sequence. ym34a11.r1 Soares infant brain 1NIB Homo sapiens cDNA clone IMAGE:50010 5', Homo sapiens mRNA sequence.	Caenorhabditis elegans cosmid C41A3. AV080151 Mus muscrilus etomach C57BI is Ladult Mus muscrilus cDNA clone.	2210413804, mas missource storings.	sapiens genomic clone Plate=2017 Col=16 Row=D, genomic survey sequence.	Homo sapiens, *** SEQUENCING IN PROGRESS ***, 2 ordered pieces.	Homo sapiens, "" SEQUENCING IN PROGRESS "", 2 ordered pieces.	B.pahangi beta-tubulin gene, complete cds.	Mouse gene for platelet activating factor receptor, complete cds.	nonio sapiens Art. I marka, compiete cas.	inycobacterium ieprae cosmia B2533. EST111890 Rat PC-12 cells, NGF-treated (9 days) Rattus sp. cDNA clone	RPNCO03, mRNA sequence.	Homo sapiens chromosome 20 clone RP4-791K14, *** SEQUENCING IN PROGRESS ***, in unordered pieces.	Homo sapiens chromosome 20 clone RP4-791K14, *** SEQUENCING IN PROGRESS *** in unordered places.	Xanthomonas campestris organic hydroperoxide resistance protein (ohr) gene, complete cds	yx19d10.r1 Soares melanocyte 2NbHM Homo sapiens cDNA clone	IMAGE:262195 5, mKNA sequence.	yx19d10.r1 Soares melanocyte 2NbHM Homo sapiens cDNA clone IMAGE:262195 5', mRNA sequence.	Deinococcus proteolyticus 40 kDa heat shock chaperone protein (dna.) gene,	for4c09.y1 Zebrafish WashU MPIMG EST Danio rerio cDNA 5' similar to	SW:DNJZ_HUMAN P31689 DNAJ PROTEIN HOMOLOG 2: ;, mRNA sequence. fd25h11;y1 Zebrafish WashU MPIMG EST Danio rerio cDNA 5' similar to SW:DNJZ_HUMAN P31689 DNAJ PROTEIN HOMOLOG 2: ;, mRNA sequence.
A1958166	AL117328	158440 AC008161	158440 AC008161	H16949	H16949	U41541 AV080151	7769970			ACUOSASS	MS6380	7/9000	A1035310	AL035310 H35255		155318 AL035685	155318 AL035685	AF036166	N25122		N25122	U93358	AI658096	AI959242
641	50502	158440	158440	465	465	37149 236	2 2	3	127587	12/38/	45/1	5 6	200	40243		155318	155318	895	620	į	620	1267	343	545
GB_EST37:Al958166	GB_PR3:HSA494016	GB_HTG2:AC008161	GB_HTG2:AC008161	GB_EST4:H16949	GB_EST4:H16949	GB_IN1:CELC41A3 GB_EST33:AV080151	10:000 W 10:00 00 00 00 00 00 00 00 00 00 00 00 00	1000 2000	GB_HTG2:AC005959	GB_H1GZ:AC005959	GB_INT:BKPTUBBA	SECTION STATES OF THE	CE PATENTONIANE DE	GB_EST4:H35255		GB_HTG1:HS791K14	GB_HTG1:HS791K14	GB_BA2:AF036166	GB_EST5:N25122		GB_ES15:N25122	GB_BA2:DPU93358	GB_EST30:AI658096	GB_EST37:A1959242
	rxa02200 1233			ra02201 486		xa02202 762			rxa02205 1002		200 30E 07E	14802303 313		rxa02431 899				xa02446 558				rxa02541 1308		

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Exemplification

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Example 1: Preparation of total genomic DNA of *Corynebacterium glutamicum* ATCC 13032

A culture of Corynebacterium glutamicum (ATCC 13032) was grown overnight 5 at 30°C with vigorous shaking in BHI medium (Difco). The cells were harvested by centrifugation, the supernatant was discarded and the cells were resuspended in 5 ml buffer-I (5% of the original volume of the culture — all indicated volumes have been calculated for 100 ml of culture volume). Composition of buffer-1: 140.34 g/l sucrose, 2.46 g/l MgSO₄ x 7H₂O₅, 10 ml/l KH₂PO₄ solution (100 g/l, adjusted to pH 6.7 with KOH), 50 ml/l M12 concentrate (10 g/l (NH₄)₂SO₄, 1 g/l NaCl, 2 g/l MgSO₄ x 7H₂O₅ 0.2 g/l CaCl₂, 0.5 g/l yeast extract (Difco), 10 ml/l trace-elements-mix (200 mg/l FeSO₄ x H₂O, 10 mg/l ZnSO₄ x 7 H₂O, 3 mg/l MnCl₂ x 4 H₂O, 30 mg/l H₁BO₁ 20 mg/l CoCl₂ x 6 H₂O, 1 mg/l NiCl₂ x 6 H₂O, 3 mg/l Na₂MoO₄ x 2 H₂O, 500 mg/l complexing agent (EDTA or critic acid), 100 ml/l vitamins-mix (0.2 mg/l biotin, 0.2 mg/l folic acid, 20 15 mg/l p-amino benzoic acid, 20 mg/l riboflavin, 40 mg/l ca-panthothenate, 140 mg/l nicotinic acid, 40 mg/l pyridoxole hydrochloride, 200 mg/l myo-inositol). Lysozyme was added to the suspension to a final concentration of 2.5 mg/ml. After an approximately 4 h incubation at 37°C, the cell wall was degraded and the resulting protoplasts are harvested by centrifugation. The pellet was washed once with 5 ml buffer-I and once with 5 ml TE-buffer (10 mM Tris-HCl, I mM EDTA, pH 8). The pellet was resuspended in 4 ml TE-buffer and 0.5 ml SDS solution (10%) and 0.5 ml NaCl solution (5 M) are added. After adding of proteinase K to a final concentration of 200 µg/ml, the suspension is incubated for ca.18 h at 37°C. The DNA was purified by extraction with phenol, phenol-chloroform-isoamylalcohol and chloroformisoamylalcohol using standard procedures. Then, the DNA was precipitated by adding 1/50 volume of 3 M sodium acetate and 2 volumes of ethanol, followed by a 30 min incubation at -20°C and a 30 min centrifugation at 12,000 rpm in a high speed centrifuge using a SS34 rotor (Sorvall). The DNA was dissolved in 1 ml TE-buffer containing 20 µg/ml RNaseA and dialysed at 4°C against 1000 ml TE-buffer for at least 3 hours. During this time, the buffer was exchanged 3 times. To aliquots of 0.4 ml of the dialysed DNA solution, 0.4 ml of 2 M LiCl and 0.8 ml of ethanol are added. After a 30

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min incubation at -20°C, the DNA was collected by centrifugation (13,000 rpm, Biofuge Fresco, Heraeus, Hanau, Germany). The DNA pellet was dissolved in TE-buffer. DNA prepared by this procedure could be used for all purposes, including southern blotting or construction of genomic libraries.

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Example 2: Construction of genomic libraries in *Escherichia coli* of *Corynebacterium glutamicum* ATCC13032.

Using DNA prepared as described in Example 1, cosmid and plasmid libraries were constructed according to known and well established methods (*see e.g.*, Sambrook, J. *et al.* (1989) "Molecular Cloning: A Laboratory Manual", Cold Spring Harbor Laboratory Press, or Ausubel, F.M. *et al.* (1994) "Current Protocols in Molecular Biology", John Wiley & Sons.)

Any plasmid or cosmid could be used. Of particular use were the plasmids pBR322 (Sutcliffe, J.G. (1979) *Proc. Natl. Acad. Sci. USA*, 75:3737-3741); pACYC177 (Change & Cohen (1978) *J. Bacteriol* 134:1141-1156), plasmids of the pBS series (pBSSK+, pBSSK- and others; Stratagene, LaJolla, USA), or cosmids as SuperCos1 (Stratagene, LaJolla, USA) or Lorist6 (Gibson, T.J., Rosenthal A. and Waterson, R.H. (1987) *Gene* 53:283-286. Gene libraries specifically for use in *C. glutamicum* may be constructed using plasmid pSL109 (Lee, H.-S. and A. J. Sinskey (1994) *J. Microbiol. Biotechnol.* 4: 256-263).

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Example 3: DNA Sequencing and Computational Functional Analysis

Genomic libraries as described in Example 2 were used for DNA sequencing according to standard methods, in particular by the chain termination method using ABI377 sequencing machines (see *e.g.*, Fleischman, R.D. *et al.* (1995) "Whole-genome Random Sequencing and Assembly of Haemophilus Influenzae Rd., *Science*, 269:496-512). Sequencing primers with the following nucleotide sequences were used: 5'-GGAAACAGTATGACCATG-3' or 5'-GTAAAACGACGGCCAGT-3'.

Example 4: In vivo Mutagenesis

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In vivo mutagenesis of Corynebacterium glutamicum can be performed by passage of plasmid (or other vector) DNA through E. coli or other microorganisms (e.g. Bacillus spp. or yeasts such as Saccharomyces cerevisiae) which are impaired in their capabilities to maintain

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the integrity of their genetic information. Typical mutator strains have mutations in the genes for the DNA repair system (e.g., mutHLS, mutD, mutT, etc.; for reference, see Rupp, W.D. (1996) DNA repair mechanisms, in: *Escherichia col*i and *Salmonella*, p. 2277-2294, ASM: Washington.) Such strains are well known to those of ordinary skill in the art. The use of such strains is illustrated, for example, in Greener, A. and Callahan, M. (1994) *Strategies* 7: 32-34.

Example 5: DNA Transfer Between *Escherichia coli* and *Corynebacterium glutamicum*

Several Corynebacterium and Brevibacterium species contain endogenous 10 plasmids (as e.g., pHM1519 or pBL1) which replicate autonomously (for review see, e.g., Martin, J.F. et al. (1987) Biotechnology, 5:137-146). Shuttle vectors for Escherichia coli and Corynebacterium glutamicum can be readily constructed by using standard vectors for E. coli (Sambrook, J. et al. (1989), "Molecular Cloning: A Laboratory Manual", Cold Spring Harbor Laboratory Press or Ausubel, F.M. et al. (1994) "Current Protocols in Molecular Biology", John Wiley & Sons) to which a origin or replication for and a 15 suitable marker from Corynebacterium glutamicum is added. Such origins of replication are preferably taken from endogenous plasmids isolated from Corvnebacterium and Brevibacterium species. Of particular use as transformation markers for these species are genes for kanamycin resistance (such as those derived from the Tn5 or Tn903 20 transposons) or chloramphenicol (Winnacker, E.L. (1987) "From Genes to Clones — Introduction to Gene Technology, VCH, Weinheim). There are numerous examples in the literature of the construction of a wide variety of shuttle vectors which replicate in both E. coli and C. glutamicum, and which can be used for several purposes, including gene overexpression (for reference, see e.g., Yoshihama, M. et al. (1985) J. Bacteriol. 162:591-597, Martin J.F. et al. (1987) Biotechnology, 5:137-146 and Eikmanns, B.J. et al. (1991) Gene, 25 102:93-98).

Using standard methods, it is possible to clone a gene of interest into one of the shuttle vectors described above and to introduce such a hybrid vector into strains of Corynebacterium glutamicum. Transformation of C. glutamicum can be achieved by protoplast transformation (Kastsumata, R. et al. (1984) J. Bacteriol. 159306-311), electroporation (Liebl, E. et al. (1989) FEMS Microbiol. Letters, 53:399-303) and in cases where special vectors are used, also by conjugation (as described e.g. in Schäfer, A et al.

(1990) J. Bacteriol. 172:1663-1666). It is also possible to transfer the shuttle vectors for *C. glutamicum* to *E. coli* by preparing plasmid DNA from *C. glutamicum* (using standard methods well-known in the art) and transforming it into *E. coli*. This transformation step can be performed using standard methods, but it is advantageous to use an Mcr-deficient *E. coli* strain, such as NM522 (Gough & Murray (1983) *J. Mol. Biol.* 166:1-19).

Genes may be overexpressed in *C. glutamicum* strains using plasmids which comprise pCG1 (U.S. Patent No. 4,617,267) or fragments thereof, and optionally the gene for kanamycin resistance from TN903 (Grindley, N.D. and Joyce, C.M. (1980) *Proc. Natl. Acad. Sci. USA* 77(12): 7176-7180). In addition, genes may be overexpressed in *C. glutamicum* strains using plasmid pSL109 (Lee, H.-S. and A. J. Sinskey (1994) *J. Microbiol. Biotechnol.* 4: 256-263).

Aside from the use of replicative plasmids, gene overexpression can also be achieved by integration into the genome. Genomic integration in *C. glutamicum* or other Corynebacterium or Brevibacterium species may be accomplished by well-known methods, such as homologous recombination with genomic region(s), restriction endonuclease mediated integration (REMI) (see, *e.g.*, DE Patent 19823834), or through the use of transposons. It is also possible to modulate the activity of a gene of interest by modifying the regulatory regions (*e.g.*, a promoter, a repressor, and/or an enhancer) by sequence modification, insertion, or deletion using site-directed methods (such as homologous recombination) or methods based on random events (such as transposon mutagenesis or REMI). Nucleic acid sequences which function as transcriptional terminators may also be inserted 3' to the coding region of one or more genes of the invention; such terminators are well-known in the art and are described, for example, in Winnacker, E.L. (1987) From Genes to Clones – Introduction to Gene Technology. VCH: Weinheim.

Example 6: Assessment of the Expression of the Mutant Protein

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Observations of the activity of a mutated protein in a transformed host cell rely on the fact that the mutant protein is expressed in a similar fashion and in a similar quantity to that of the wild-type protein. A useful method to ascertain the level of transcription of the mutant gene (an indicator of the amount of mRNA available for translation to the gene product) is to perform a Northern blot (for reference see, for example, Ausubel *et al.*)

(1988) Current Protocols in Molecular Biology, Wiley: New York), in which a primer designed to bind to the gene of interest is labeled with a detectable tag (usually radioactive or chemiluminescent), such that when the total RNA of a culture of the organism is extracted, run on gel, transferred to a stable matrix and incubated with this probe, the binding and quantity of binding of the probe indicates the presence and also the quantity of mRNA for this gene. This information is evidence of the degree of transcription of the mutant gene. Total cellular RNA can be prepared from *Corynebacterium glutamicum* by several methods, all well-known in the art, such as that described in Bormann, E.R. *et al.* (1992) *Mol. Microbiol.* 6: 317-326.

To assess the presence or relative quantity of protein translated from this mRNA, standard techniques, such as a Western blot, may be employed (see, for example, Ausubel et al. (1988) Current Protocols in Molecular Biology, Wiley: New York). In this process, total cellular proteins are extracted, separated by gel electrophoresis, transferred to a matrix such as nitrocellulose, and incubated with a probe, such as an antibody, which specifically binds to the desired protein. This probe is generally tagged with a chemiluminescent or colorimetric label which may be readily detected. The presence and quantity of label observed indicates the presence and quantity of the desired mutant protein present in the cell.

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20 Example 7: Growth of Genetically Modified *Corynebacterium glutamicum* — Media and Culture Conditions

Genetically modified *Corynebacteria* are cultured in synthetic or natural growth media. A number of different growth media for Corynebacteria are both well-known and readily available (Lieb *et al.* (1989) *Appl. Microbiol. Biotechnol.*, 32:205-210; von der Osten *et al.* (1998) *Biotechnology Letters*, 11:11-16; Patent DE 4,120,867; Liebl (1992) "The Genus *Corynebacterium*, in: The Procaryotes, Volume II, Balows, A. *et al.*, eds. Springer-Verlag). These media consist of one or more carbon sources, nitrogen sources, inorganic salts, vitamins and trace elements. Preferred carbon sources are sugars, such as mono-, di-, or polysaccharides. For example, glucose, fructose, mannose, galactose, ribose, sorbose, ribulose, lactose, maltose, sucrose, raffinose, starch or cellulose serve as very good carbon sources. It is also possible to supply sugar to the media via complex compounds such as molasses or other by-products from sugar refinement. It can also be

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advantageous to supply mixtures of different carbon sources. Other possible carbon sources are alcohols and organic acids, such as methanol, ethanol, acetic acid or lactic acid. Nitrogen sources are usually organic or inorganic nitrogen compounds, or materials which contain these compounds. Exemplary nitrogen sources include ammonia gas or ammonia salts, such as NH₄Cl or (NH₄)₂SO₄, NH₄OH, nitrates, urea, amino acids or complex nitrogen sources like corn steep liquor, soy bean flour, soy bean protein, yeast extract, meat extract and others.

Inorganic salt compounds which may be included in the media include the chloride-, phosphorous- or sulfate- salts of calcium, magnesium, sodium, cobalt, molybdenum, potassium, manganese, zinc, copper and iron. Chelating compounds can be added to the medium to keep the metal ions in solution. Particularly useful chelating compounds include dihydroxyphenols, like catechol or protocatechuate, or organic acids, such as citric acid. It is typical for the media to also contain other growth factors, such as vitamins or growth promoters, examples of which include biotin, riboflavin, thiamin, folic acid, nicotinic acid, pantothenate and pyridoxin. Growth factors and salts frequently originate from complex media components such as yeast extract, molasses, corn steep liquor and others. The exact composition of the media compounds depends strongly on the immediate experiment and is individually decided for each specific case. Information about media optimization is available in the textbook "Applied Microbiol. Physiology, A 20 Practical Approach (eds. P.M. Rhodes, P.F. Stanbury, IRL Press (1997) pp. 53-73, ISBN 0 19 963577 3). It is also possible to select growth media from commercial suppliers, like standard 1 (Merck) or BHI (grain heart infusion, DIFCO) or others.

All medium components are sterilized, either by heat (20 minutes at 1.5 bar and 121°C) or by sterile filtration. The components can either be sterilized together or, if necessary, separately. All media components can be present at the beginning of growth, or they can optionally be added continuously or batchwise.

Culture conditions are defined separately for each experiment. The temperature should be in a range between 15°C and 45°C. The temperature can be kept constant or can be altered during the experiment. The pH of the medium should be in the range of 5 to 8.5, preferably around 7.0, and can be maintained by the addition of buffers to the media. An exemplary buffer for this purpose is a potassium phosphate buffer. Synthetic buffers such as MOPS, HEPES, ACES and others can alternatively or simultaneously be used. It

is also possible to maintain a constant culture pH through the addition of NaOH or NH₄OH during growth. If complex medium components such as yeast extract are utilized, the necessity for additional buffers may be reduced, due to the fact that many complex compounds have high buffer capacities. If a fermentor is utilized for culturing the microorganisms, the pH can also be controlled using gaseous ammonia.

The incubation time is usually in a range from several hours to several days. This time is selected in order to permit the maximal amount of product to accumulate in the broth. The disclosed growth experiments can be carried out in a variety of vessels, such as microtiter plates, glass tubes, glass flasks or glass or metal fermentors of different sizes.

For screening a large number of clones, the microorganisms should be cultured in microtiter plates, glass tubes or shake flasks, either with or without baffles. Preferably 100 ml shake flasks are used, filled with 10% (by volume) of the required growth medium. The flasks should be shaken on a rotary shaker (amplitude 25 mm) using a speed-range of 100 – 300 rpm. Evaporation losses can be diminished by the maintenance of a humid atmosphere; alternatively, a mathematical correction for evaporation losses should be performed.

If genetically modified clones are tested, an unmodified control clone or a control clone containing the basic plasmid without any insert should also be tested. The medium is inoculated to an OD₆₀₀ of O.5 – 1.5 using cells grown on agar plates, such as CM plates (10 g/l glucose, 2,5 g/l NaCl, 2 g/l urea, 10 g/l polypeptone, 5 g/l yeast extract, 5 g/l meat extract, 22 g/l NaCl, 2 g/l urea, 10 g/l polypeptone, 5 g/l yeast extract, 5 g/l meat extract, 22 g/l agar, pH 6.8 with 2M NaOH) that had been incubated at 30°C. Inoculation of the media is accomplished by either introduction of a saline suspension of *C. glutamicum* cells from CM plates or addition of a liquid preculture of this bacterium.

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Example 8 - In vitro Analysis of the Function of Mutant Proteins

The determination of activities and kinetic parameters of enzymes is well established in the art. Experiments to determine the activity of any given altered enzyme must be tailored to the specific activity of the wild-type enzyme, which is well within the ability of one of ordinary skill in the art. Overviews about enzymes in general, as well as specific details concerning structure, kinetics, principles, methods, applications and examples for the determination of many enzyme activities may be

found, for example, in the following references: Dixon, M., and Webb, E.C., (1979) Enzymes. Longmans: London; Fersht, (1985) Enzyme Structure and Mechanism. Freeman: New York; Walsh, (1979) Enzymatic Reaction Mechanisms. Freeman: San Francisco; Price, N.C., Stevens, L. (1982) Fundamentals of Enzymology. Oxford Univ.

5 Press: Oxford; Boyer, P.D., ed. (1983) The Enzymes, 3rd ed. Academic Press: New York; Bisswanger, H., (1994) Enzymkinetik, 2nd ed. VCH: Weinheim (ISBN 3527300325); Bergmeyer, H.U., Bergmeyer, J., Graßl, M., eds. (1983-1986) Methods of Enzymatic Analysis, 3rd ed., vol. I-XII, Verlag Chemie: Weinheim; and Ullmann's Encyclopedia of Industrial Chemistry (1987) vol. A9, "Enzymes". VCH: Weinheim, p. 352-363.

The activity of proteins which bind to DNA can be measured by several well-established methods, such as DNA band-shift assays (also called gel retardation assays). The effect of such proteins on the expression of other molecules can be measured using reporter gene assays (such as that described in Kolmar, H. *et al.* (1995) *EMBO J.* 14: 3895-3904 and references cited therein). Reporter gene test systems are well known and established for applications in both pro- and eukaryotic cells, using enzymes such as beta-galactosidase, green fluorescent protein, and several others.

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The determination of activity of membrane-transport proteins can be performed according to techniques such as those described in Gennis, R.B. (1989) "Pores, Channels and Transporters", in Biomembranes, Molecular Structure and Function, Springer: Heidelberg, p. 85-137; 199-234; and 270-322.

Example 9: Analysis of Impact of Mutant Protein on the Production of the Desired Product

The effect of the genetic modification in *C. glutamicum* on production of a desired compound (such as an amino acid) can be assessed by growing the modified microorganism under suitable conditions (such as those described above) and analyzing the medium and/or the cellular component for increased production of the desired product (*i.e.*, an amino acid). Such analysis techniques are well known to one of ordinary skill in the art, and include spectroscopy, thin layer chromatography, staining methods of various kinds, enzymatic and microbiological methods, and analytical chromatography such as high performance liquid chromatography (see, for example,

Ullman, Encyclopedia of Industrial Chemistry, vol. A2, p. 89-90 and p. 443-613, VCH: Weinheim (1985); Fallon, A. et al., (1987) "Applications of HPLC in Biochemistry" in: Laboratory Techniques in Biochemistry and Molecular Biology, vol. 17; Rehm et al. (1993) Biotechnology, vol. 3, Chapter III: "Product recovery and purification", page 469-714, VCH: Weinheim; Belter, P.A. et al. (1988) Bioseparations: downstream processing for biotechnology, John Wiley and Sons; Kennedy, J.F. and Cabral, J.M.S. (1992) Recovery processes for biological materials, John Wiley and Sons; Shaeiwitz, J.A. and Henry, J.D. (1988) Biochemical separations, in: Ulmann's Encyclopedia of Industrial Chemistry, vol. B3, Chapter 11, page 1-27, VCH: Weinheim; and Dechow, F.J. (1989) Separation and purification techniques in biotechnology, Noyes Publications.)

In addition to the measurement of the final product of fermentation, it is also possible to analyze other components of the metabolic pathways utilized for the production of the desired compound, such as intermediates and side-products, to determine the overall yield, production, and/or efficiency of production of the compound. Analysis methods include measurements of nutrient levels in the medium (e.g., sugars, hydrocarbons, nitrogen sources, phosphate, and other ions), measurements of biomass composition and growth, analysis of the production of common metabolites of biosynthetic pathways, and measurement of gasses produced during fermentation. Standard methods for these measurements are outlined in Applied Microbial Physiology, A Practical Approach, P.M. Rhodes and P.F. Stanbury, eds., IRL Press, p. 103-129; 131-163; and 165-192 (ISBN: 0199635773) and references cited therein.

Example 10: Purification of the Desired Product from C. glutamicum Culture

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Recovery of the desired product from the *C. glutamicum* cells or supernatant of the above-described culture can be performed by various methods well known in the art. If the desired product is not secreted from the cells, the cells can be harvested from the culture by low-speed centrifugation, the cells can be lysed by standard techniques, such as mechanical force or sonication. The cellular debris is removed by centrifugation, and the supernatant fraction containing the soluble proteins is retained for further purification of the desired compound. If the product is secreted from the *C. glutamicum*

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cells, then the cells are removed from the culture by low-speed centrifugation, and the supernate fraction is retained for further purification.

The supernatant fraction from either purification method is subjected to chromatography with a suitable resin, in which the desired molecule is either retained on a chromatography resin while many of the impurities in the sample are not, or where the impurities are retained by the resin while the sample is not. Such chromatography steps may be repeated as necessary, using the same or different chromatography resins. One of ordinary skill in the art would be well-versed in the selection of appropriate chromatography resins and in their most efficacious application for a particular molecule to be purified. The purified product may be concentrated by filtration or ultrafiltration, and stored at a temperature at which the stability of the product is maximized.

There are a wide array of purification methods known to the art and the preceding method of purification is not meant to be limiting. Such purification techniques are described, for example, in Bailey, J.E. & Ollis, D.F. Biochemical Engineering Fundamentals, McGraw-Hill: New York (1986).

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The identity and purity of the isolated compounds may be assessed by techniques standard in the art. These include high-performance liquid chromatography (HPLC), spectroscopic methods, staining methods, thin layer chromatography, NIRS, enzymatic assay, or microbiologically. Such analysis methods are reviewed in: Patek *et al.* (1994) *Appl. Environ. Microbiol.* 60: 133-140; Malakhova *et al.* (1996) *Biotekhnologiya* 11: 27-32; and Schmidt *et al.* (1998) *Bioprocess Engineer*. 19: 67-70. Ulmann's Encyclopedia of Industrial Chemistry, (1996) vol. A27, VCH: Weinheim, p. 89-90, p. 521-540, p. 540-547, p. 559-566, 575-581 and p. 581-587; Michal, G. (1999) Biochemical Pathways: An Atlas of Biochemistry and Molecular Biology, John Wiley and Sons; Fallon, A. *et al.* (1987) Applications of HPLC in Biochemistry in: Laboratory Techniques in Biochemistry and Molecular Biology, vol. 17.

EXAMPLE 11: Cloning of a *Corynebacterium glutamicum* Gene Involved in Lincomycin Resistance Using a Reporter Gene Approach

A. Identification of the Gene Encoding the LMRB Protein

Plasmid pSL130 was constructed by ligation of the aceB promoter region (paceB) of C. glutamicum (Kim, H.J. et al. (1997) J. Microbiol. Biotechnol. 7: 287-292) into the polylinker of the lac operon fusion vector pRS415, which lacks a promoter (Simon, R.W. et al. (1987) Gene 53: 85-96). Plasmid pSL145 was constructed by ligating the resulting paceB-lac region into the E. coli cloning vector pACYC184. E. coli DH5αF' was transformed with pSL145 and the resulting strain was used as a host for screening of a genomic C. glutamicum library (in pSL109).

Transformants were screened by growth on agar medium containing 5-bromo-4chloro-3-indolyl-beta-D-glalactopyranoside (X-Gal). A white colony, containing DNA 10 influencing lacZ expression, was selected for further analysis. This clone was found to contain a 4 kB fragment from the gene library. Subclones were constructed in pSL109 and a subclone which retained the white phenotype on X-Gal plates was identified. This subclone was found to contain a 2.6 kB BamH1-XhoI fragment (plasmid pSL149-5). The fragment was sequenced and identified as a membrane protein-encoding gene (LMRB gene).

The 1442 nucleotides of the coding sequence of the LMRB gene encode a polypeptide of 481 amino acid residues with a high percentage of hydrophobic amino acids. A Genbank search determined that the LMRB protein is 40% identical to the protein product of the lmrB gene from Bacillus subtilis (Genbank Accession AL009126, TREMBL Accession P94422), as determined using a CLUSTAL W analysis (using standard parameters).

The LMRN protein contains a sequence pattern: 158-A-P-A-L-G-P-T-L-S-G-167 (SEQ ID NO:301), which resembles the known multi-drug-resistance-protein consensus motif G-X-X-G-P-X-X-G-G (SEQ ID NO:302) (Paulsen, I.T., and Skurray, R.A. (1993) Gene 124: 1-11). Therefore, the LMRB protein was classified as a drug resistance protein.

B. In vivo Analysis of lmrB Function

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The lmrB gene was overexpressed in C. glutamicum ASO19E12 (Kim, H.J. et al. (1997) J. Microbiol. Biotechnol. 7: 287-292) using the plasmid pSL149-5, described above.

Disruption of the LMRB gene was accomplished by use of the vector pSL18-lmrB. This vector was constructed as follows: an internal fragment of the LMRB gene was amplified by PCR under standard conditions using primers 5'-CTCCAGGATTGCTCCGAAGG-3' (SEQ ID NO:303) and 5'-

5 CACAGTGGTTGACCACTGGC-3' (SEQ ID NO:304). The resulting PCR product was treated with T7 DNA polymerase and T7 polynucleotide kinase, and was cloned into the Smal site of plasmid pSL18 (Kim, Y.H. and H.-S. Lee (1996) *J. Microbiol. Biotechnol.* 6: 315-320). The disruption of the LMRB gene in *C. glutamicum* ASO19E12 was performed by conjugation, as previously described (Schwarzer and Puhler (1991) *Bio/Technology* 9:84-87).

C. glutamicum cells transformed with pSL149-5 displayed similar resistances as untransformed cells against erythromycin, penicillin G, tetracycline, chloramphenicol, spectinomycin, nalidixic acid, gentamycin, streptomycin, ethidium bromide, carbonyl cyanide m-chlorophenylhydrazone (CCCP), and sodium dodecyl sulfate. Significant differences were observed, however, in the resistance of transformed and untransformed cells to lincomycin.

LMRB-overexpressing *C. glutamicum* cells were found to be able to grow in the presence of 20 µg/ml lincomycin. In contrast, cells which do not overexpress LMRB (or cells carrying a LMRB disruption) were not able to grow on agar media containing 5 µg/ml lincomycin. This effect was clearly visible in liquid culture. LMRB overexpression led to a 9-fold increased resistance (compared to wild-type) against lincomycin and LMRB disruption resulted in a decreased resistance (28% of wild-type) to this antibiotic.

25 Example 12: Analysis of the Gene Sequences of the Invention

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The comparison of sequences and determination of percent homology between two sequences are art-known techniques, and can be accomplished using a mathematical algorithm, such as the algorithm of Karlin and Altschul (1990) *Proc. Natl. Acad. Sci.* USA 87:2264-68, modified as in Karlin and Altschul (1993) *Proc. Natl. Acad. Sci.* USA 90:5873-77. Such an algorithm is incorporated into the NBLAST and XBLAST programs (version 2.0) of Altschul, *et al.* (1990) *J. Mol. Biol.* 215:403-10. BLAST nucleotide searches can be performed with the NBLAST program, score = 100,

wordlength = 12 to obtain nucleotide sequences homologous to SRT nucleic acid molecules of the invention. BLAST protein searches can be performed with the XBLAST program, score = 50, wordlength = 3 to obtain amino acid sequences homologous to SRT protein molecules of the invention. To obtain gapped alignments for comparison purposes, Gapped BLAST can be utilized as described in Altschul *et al.*, (1997) *Nucleic Acids Res.* 25(17):3389-3402. When utilizing BLAST and Gapped BLAST programs, one of ordinary skill in the art will know how to optimize the parameters of the program (*e.g.*, XBLAST and NBLAST) for the specific sequence being analyzed.

Another example of a mathematical algorithm utilized for the comparison of sequences is the algorithm of Meyers and Miller ((1988) Comput. Appl. Biosci. 4: 11-17). Such an algorithm is incorporated into the ALIGN program (version 2.0) which is part of the GCG sequence alignment software package. When utilizing the ALIGN program for comparing amino acid sequences, a PAM120 weight residue table, a gap length penalty of 12, and a gap penalty of 4 can be used. Additional algorithms for sequence analysis are known in the art, and include ADVANCE and ADAM. described in Torelli and Robotti (1994) Comput. Appl. Biosci. 10:3-5; and FASTA, described in Pearson and Lipman (1988) P.N.A.S. 85:2444-8.

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The percent homology between two amino acid sequences can also be accomplished using the GAP program in the GCG software package (available at http://www.gcg.com), using either a Blosum 62 matrix or a PAM250 matrix, and a gap weight of 12, 10, 8, 6, or 4 and a length weight of 2, 3, or 4. The percent homology between two nucleic acid sequences can be accomplished using the GAP program in the GCG software package, using standard parameters, such as a gap weight of 50 and a length weight of 3.

A comparative analysis of the gene sequences of the invention with those present in Genbank has been performed using techniques known in the art (see, e.g., Bexevanis and Ouellette, eds. (1998) Bioinformatics: A Practical Guide to the Analysis of Genes and Proteins. John Wiley and Sons: New York). The gene sequences of the invention were compared to genes present in Genbank in a three-step process. In a first step, a BLASTN analysis (e.g., a local alignment analysis) was performed for each of the sequences of the invention against the nucleotide sequences present in Genbank, and the

top 500 hits were retained for further analysis. A subsequent FASTA search (e.g., a combined local and global alignment analysis, in which limited regions of the sequences are aligned) was performed on these 500 hits. Each gene sequence of the invention was subsequently globally aligned to each of the top three FASTA hits, using the GAP program in the GCG software package (using standard parameters). In order to obtain correct results, the length of the sequences extracted from Genbank were adjusted to the length of the query sequences by methods well-known in the art. The results of this analysis are set forth in Table 4. The resulting data is identical to that which would have been obtained had a GAP (global) analysis alone been performed on each of the genes of the invention in comparison with each of the references in Genbank, but required significantly reduced computational time as compared to such a database-wide GAP (global) analysis. Sequences of the invention for which no alignments above the cutoff values were obtained are indicated on Table 4 by the absence of alignment information. It will further be understood by one of ordinary skill in the art that the GAP alignment homology percentages set forth in Table 4 under the heading "% homology (GAP)" are listed in the European numerical format, wherein a ',' represents a decimal point. For example, a value of "40,345" in this column represents "40.345%".

Example 13: Construction and Operation of DNA Microarrays

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The sequences of the invention may additionally be used in the construction and application of DNA microarrays (the design, methodology, and uses of DNA arrays are well known in the art, and are described, for example, in Schena, M. et al. (1995)

Science 270: 467-470; Wodicka, L. et al. (1997) Nature Biotechnology 15: 1359-1367;

DeSaizieu, A. et al. (1998) Nature Biotechnology 16: 45-48; and DeRisi, J.L. et al.

(1997) Science 278: 680-686).

DNA microarrays are solid or flexible supports consisting of nitrocellulose, nylon, glass, silicone, or other materials. Nucleic acid molecules may be attached to the surface in an ordered manner. After appropriate labeling, other nucleic acids or nucleic acid mixtures can be hybridized to the immobilized nucleic acid molecules, and the label may be used to monitor and measure the individual signal intensities of the hybridized molecules at defined regions. This methodology allows the simultaneous quantification of the relative or absolute amount of all or selected nucleic acids in the applied nucleic

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acid sample or mixture. DNA microarrays, therefore, permit an analysis of the expression of multiple (as many as 6800 or more) nucleic acids in parallel (see, e.g., Schena, M. (1996) *BioEssays* 18(5): 427-431).

The sequences of the invention may be used to design oligonucleotide primers which are able to amplify defined regions of one or more *C. glutamicum* genes by a nucleic acid amplification reaction such as the polymerase chain reaction. The choice and design of the 5' or 3' oligonucleotide primers or of appropriate linkers allows the covalent attachment of the resulting PCR products to the surface of a support medium described above (and also described, for example, Schena, M. *et al.* (1995) *Science* 270: 467-470).

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Nucleic acid microarrays may also be constructed by *in situ* oligonucleotide synthesis as described by Wodicka, L. *et al.* (1997) *Nature Biotechnology* 15: 1359-1367. By photolithographic methods, precisely defined regions of the matrix are exposed to light. Protective groups which are photolabile are thereby activated and undergo nucleotide addition, whereas regions that are masked from light do not undergo any modification. Subsequent cycles of protection and light activation permit the synthesis of different oligonucleotides at defined positions. Small, defined regions of the genes of the invention may be synthesized on microarrays by solid phase oligonucleotide synthesis.

The nucleic acid molecules of the invention present in a sample or mixture of nucleotides may be hybridized to the microarrays. These nucleic acid molecules can be labeled according to standard methods. In brief, nucleic acid molecules (e.g., mRNA molecules or DNA molecules) are labeled by the incorporation of isotopically or fluorescently labeled nucleotides, e.g., during reverse transcription or DNA synthesis.

Hybridization of labeled nucleic acids to microarrays is described (e.g., in Schena, M. et al. (1995) supra; Wodicka, L. et al. (1997), supra; and DeSaizieu A. et al. (1998), supra). The detection and quantification of the hybridized molecule are tailored to the specific incorporated label. Radioactive labels can be detected, for example, as described in Schena, M. et al. (1995) supra) and fluorescent labels may be detected, for example, by the method of Shalon et al. (1996) Genome Research 6: 639-645).

The application of the sequences of the invention to DNA microarray technology, as described above, permits comparative analyses of different strains of *C*.

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glutamicum or other Corynebacteria. For example, studies of inter-strain variations based on individual transcript profiles and the identification of genes that are important for specific and/or desired strain properties such as pathogenicity, productivity and stress tolerance are facilitated by nucleic acid array methodologies. Also, comparisons of the profile of expression of genes of the invention during the course of a fermentation reaction are possible using nucleic acid array technology.

Example 14: Analysis of the Dynamics of Cellular Protein Populations (Proteomics)

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The genes, compositions, and methods of the invention may be applied to study the interactions and dynamics of populations of proteins, termed 'proteomics'. Protein populations of interest include, but are not limited to, the total protein population of *C. glutamicum* (e.g., in comparison with the protein populations of other organisms), those proteins which are active under specific environmental or metabolic conditions (e.g., during fermentation, at high or low temperature, or at high or low pH), or those proteins which are active during specific phases of growth and development.

Protein populations can be analyzed by various well-known techniques, such as gel electrophoresis. Cellular proteins may be obtained, for example, by lysis or extraction, and may be separated from one another using a variety of electrophoretic techniques. Sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE) separates proteins largely on the basis of their molecular weight. Isoelectric focusing polyacrylamide gel electrophoresis (IEF-PAGE) separates proteins by their isoelectric point (which reflects not only the amino acid sequence but also posttranslational modifications of the protein). Another, more preferred method of protein analysis is the consecutive combination of both IEF-PAGE and SDS-PAGE, known as 2-D-gel electrophoresis (described, for example, in Hermann *et al.* (1998) *Electrophoresis* 19: 3217-3221; Fountoulakis *et al.* (1998) *Electrophoresis* 19: 1193-1202; Langen *et al.* (1997) *Electrophoresis* 18: 1184-1192; Antelmann *et al.* (1997) *Electrophoresis* 18: 1451-1463). Other separation techniques may also be utilized for protein separation, such as capillary gel electrophoresis; such techniques are well known in the art.

Proteins separated by these methodologies can be visualized by standard techniques, such as by staining or labeling. Suitable stains are known in the art, and

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include Coomassie Brilliant Blue, silver stain, or fluorescent dyes such as Sypro Ruby (Molecular Probes). The inclusion of radioactively labeled amino acids or other protein precursors (e.g., ³⁵S-methionine, ³⁵S-cysteine, ¹⁴C-labelled amino acids, ¹⁵N-amino acids, ¹⁵NO₃ or ¹⁵NH₄⁺ or ¹³C-labelled amino acids) in the medium of *C. glutamicum* permits the labeling of proteins from these cells prior to their separation. Similarly, fluorescent labels may be employed. These labeled proteins can be extracted, isolated and separated according to the previously described techniques.

Proteins visualized by these techniques can be further analyzed by measuring the amount of dye or label used. The amount of a given protein can be determined quantitatively using, for example, optical methods and can be compared to the amount of other proteins in the same gel or in other gels. Comparisons of proteins on gels can be made, for example, by optical comparison, by spectroscopy, by image scanning and analysis of gels, or through the use of photographic films and screens. Such techniques are well-known in the art.

To determine the identity of any given protein, direct sequencing or other standard techniques may be employed. For example, N- and/or C-terminal amino acid sequencing (such as Edman degradation) may be used, as may mass spectrometry (in particular MALDI or ESI techniques (see, e.g., Langen et al. (1997) Electrophoresis 18: 1184-1192)). The protein sequences provided herein can be used for the identification of C. glutamicum proteins by these techniques.

The information obtained by these methods can be used to compare patterns of protein presence, activity, or modification between different samples from various biological conditions (e.g., different organisms, time points of fermentation, media conditions, or different biotopes, among others). Data obtained from such experiments alone, or in combination with other techniques, can be used for various applications, such as to compare the behavior of various organisms in a given (e.g., metabolic) situation, to increase the productivity of strains which produce fine chemicals or to increase the efficiency of the production of fine chemicals.

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Equivalents

Those of ordinary skill in the art will recognize, or will be able to ascertain using no more than routine experimentation, many equivalents to the specific embodiments of the invention described herein. Such equivalents are intended to be encompassed by the following claims.

What is claimed:

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- 1. An isolated nucleic acid molecule from *Corynebacterium glutamicum* encoding a stress, resistance, or tolerance gene, or a portion thereof, provided that the nucleic acid molecule does not consist of any of the F-designated genes set forth in Table 1.
 - 2. The isolated nucleic acid molecule of claim 1, wherein said stress, resistance, or tolerance gene is selected from the group consisting of nucleic acid molecules involved in a stress response, tolerance, or resistance to temperature stresses, pH stresses, oxygen stresses, osmotic stresses, toxic chemicals, oxygen radicals, antibiotics, or to lincomycin.
- 3. An isolated Corynebacterium glutamicum nucleic acid molecule selected from the group consisting of those sequences set forth as odd-numbered SEQ ID NOs of the Sequence Listing, or a portion thereof, provided that the nucleic acid molecule does not consist of any of the F-designated genes set forth in Table 1.
- 4. An isolated nucleic acid molecule which encodes a polypeptide sequence selected from the group consisting of those sequences set forth as even-numbered SEQ ID NOs of the Sequence Listing, provided that the nucleic acid molecule does not consist of any of the F-designated genes set forth in Table 1.
- 5. An isolated nucleic acid molecule which encodes a naturally occurring allelic variant of a polypeptide selected from the group of amino acid sequences consisting of those sequences set forth as even-numbered SEQ ID NOs of the Sequence Listing, provided that the nucleic acid molecule does not consist of any of the F-designated genes set forth in Table 1.
- 30 6. An isolated nucleic acid molecule comprising a nucleotide sequence which is at least 50% homologous to a nucleotide sequence selected from the group consisting of those sequences set forth as odd-numbered SEQ ID NOs of the Sequence Listing, or

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a portion thereof, provided that the nucleic acid molecule does not consist of any of the F-designated genes set forth in Table 1.

- 7. An isolated nucleic acid molecule comprising a fragment of at least 15 nucleotides of a nucleic acid comprising a nucleotide sequence selected from the group consisting of those sequences set forth as odd-numbered SEQ ID NOs of the Sequence Listing, provided that the nucleic acid molecule does not consist of any of the F-designated genes set forth in Table 1.
- 10 8. An isolated nucleic acid molecule which hybridizes to the nucleic acid molecule of any one of claims 1-7 under stringent conditions.
- 9. An isolated nucleic acid molecule comprising the nucleic acid molecule of any one of claims 1-8 or a portion thereof and a nucleotide sequence encoding a heterologous polypeptide.
 - 10. A vector comprising the nucleic acid molecule of any one of claims 1-9.
 - 11. The vector of claim 10, which is an expression vector.

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- 12. A host cell transfected with the expression vector of claim 11.
- 13. The host cell of claim 12, wherein said cell is a microorganism.
- 25 14. The host cell of claim 13, wherein said cell belongs to the genus Corynebacterium or Brevibacterium.
 - 15. The host cell of claim 12, wherein the expression of said nucleic acid molecule results in the modulation in production of a fine chemical from said cell.

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16. The host cell of claim 15, wherein said fine chemical is selected from the group consisting of: organic acids, proteinogenic and nonproteinogenic amino acids, purine

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and pyrimidine bases, nucleosides, nucleotides, lipids, saturated and unsaturated fatty acids, diols, carbohydrates, aromatic compounds, vitamins, cofactors, polyketides, and enzymes.

- 17. A method of producing a polypeptide comprising culturing the host cell of claim 12 in an appropriate culture medium to, thereby, produce the polypeptide.
 - 18. An isolated stress, resistance, or tolerance polypeptide from *Corynebacterium glutamicum*, or a portion thereof.

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19. The protein of claim 18, wherein said stress, resistance, or tolerance polypeptide is selected from the group consisting of proteins involved in a stress response, tolerance, or resistance to temperature stresses, pH stresses, oxygen stresses, osmotic stresses, toxic chemicals, oxygen radicals, antibiotics, or to lincomycin.

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20. An isolated polypeptide comprising an amino acid sequence selected from the group consisting of those sequences set forth as even-numbered SEQ ID NOs of the Sequence Listing, provided that the amino acid sequence is not encoded by any of the F-designated genes set forth in Table 1.

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- 21. An isolated polypeptide comprising a naturally occurring allelic variant of a polypeptide comprising an amino acid sequence selected from the group consisting of those sequences set forth as even-numbered SEQ ID NOs of the Sequence Listing, or a portion thereof, provided that the amino acid sequence is not encoded by any of the F-designated genes set forth in Table 1.
- 22. The isolated polypeptide of any of claims 18-21, further comprising heterologous amino acid sequences.
- 30 23. An isolated polypeptide which is encoded by a nucleic acid molecule comprising a nucleotide sequence which is at least 50% homologous to a nucleic acid selected from the group consisting of those sequences set forth as odd-numbered SEQ ID

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NOs of the Sequence Listing,, provided that the nucleic acid molecule does not consist of any of the F-designated nucleic acid molecules set forth in Table 1.

- 24. An isolated polypeptide comprising an amino acid sequence which is at least 50%
 homologous to an amino acid sequence selected from the group consisting of those sequences set forth as even-numbered SEQ ID NOs of the Sequence Listing, provided that the amino acid sequence is not encoded by any of the F-designated genes set forth in Table 1.
- 10 25. A method for producing a fine chemical, comprising culturing a cell containing a vector of claim 12 such that the fine chemical is produced.
 - 26. The method of claim 25, wherein said method further comprises the step of recovering the fine chemical from said culture.

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- 27. The method of claim 25, wherein said method further comprises the step of transfecting said cell with the vector of claim 11 to result in a cell containing said vector.
- 20 28. The method of claim 25, wherein said cell belongs to the genus *Corynebacterium* or *Brevibacterium*.
 - 29. The method of claim 25, wherein said cell is selected from the group consisting of: Corynebacterium glutamicum, Corynebacterium herculis, Corynebacterium, lilium,
- 25 Corynebacterium acetoacidophilum, Corynebacterium acetoglutamicum, Corynebacterium acetophilum, Corynebacterium ammoniagenes, Corynebacterium fujiokense, Corynebacterium nitrilophilus, Brevibacterium ammoniagenes, Brevibacterium butanicum, Brevibacterium divaricatum, Brevibacterium flavum, Brevibacterium healii, Brevibacterium ketoglutamicum, Brevibacterium
- 30 ketosoreductum, Brevibacterium lactofermentum, Brevibacterium linens, Brevibacterium paraffinolyticum, and those strains set forth in Table 3.

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- 30. The method of claim 25, wherein expression of the nucleic acid molecule from said vector results in modulation of production of said fine chemical.
- 31. The method of claim 25, wherein said fine chemical is selected from the group consisting of: organic acids, proteinogenic and nonproteinogenic amino acids, purine and pyrimidine bases, nucleosides, nucleotides, lipids, saturated and unsaturated fatty acids, diols, carbohydrates, aromatic compounds, vitamins, cofactors, polyketides and enzymes.
- 10 32. The method of claim 25, wherein said fine chemical is an amino acid.
 - 33. The method of claim 32, wherein said amino acid is drawn from the group consisting of: lysine, glutamate, glutamine, alanine, aspartate, glycine, serine, threonine, methionine, cysteine, valine, leucine, isoleucine, arginine, proline, histidine, tyrosine, phenylalanine, and tryptophan.
 - 34. A method for producing a fine chemical, comprising culturing a cell whose genomic DNA has been altered by the inclusion of a nucleic acid molecule of any one of claims 1-9.

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- 35. A method for diagnosing the presence or activity of Corynebacterium diphtheriae in a subject, comprising detecting the presence of one or more SEQ ID NOs 1 through 304 of the Sequence Listing in the subject, provided that the sequences are not or are not encoded by any of the F-designated sequences set forth in Table 1, thereby diagnosing the presence or activity of Corynebacterium diphtheriae in the subject.
- 36. A host cell comprising a nucleic acid molecule selected from the group consisting of the nucleic acid molecules set forth as odd-numbered SEQ ID NOs of the Sequence Listing, wherein the nucleic acid molecule is disrupted.

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37. A host cell comprising a nucleic acid molecule selected from the group consisting of the nucleic acid molecules set forth as odd-numbered SEQ ID NOs of the

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Sequence Listing , wherein the nucleic acid molecule comprises one or more nucleic acid modifications from the sequence set forth as odd-numbered SEQ ID NOs of the Sequence Listing .

38. A host cell comprising a nucleic acid molecule selected from the group consisting of the nucleic acid molecules set as odd-numbered SEQ ID NOs of the Sequence Listing, wherein the regulatory region of the nucleic acid molecule is modified relative to the wild-type regulatory region of the molecule.

SEQUENCE LISTING

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		ag acc		Pro											163
		t tcg eu Ser 25	Ile												211
	hr II	t ctg Le Leu 10													259
Val P		a act u Thr													307
		g gtg il Val													355
		g atc r Ile													403
ttg ac Leu T		g gcg a Ala 105													451
atc g															499

120 125 130

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		tcc Ser														595
		gtc Val														643
		ccg Pro														691
		atc Ile 200														739
		tcg Ser			_				_							787
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Leu	Gly	aag Lys	Gln 265	Asp	Lys	Ala	Leu	Met 270	Asp	Leu	Arg	Ala	Phe 275	Lys	Val	931
		ttc Phe 280														979
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		cgt Arg														1171

Ala					ttt Phe											1219
					gtg Val											1267
	Leu				gct Ala 395											1315
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					gcg Ala											1459
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aaa	atgg	ggc a	aga													1566
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gtg gag tac ttg ctt ctc tcc gct cgt gac atc ctc gca atc gtc gag 345 Val Glu Tyr Leu Leu Leu Ser Ala Arg Asp Ile Leu Ala Ile Val Glu 90 371 aag taggggataa gttcatggca aag Lys <210> 4 <211> 99 <212> PRT <213> Corynebacterium glutamicum Val Ala Asn Val Asn Ile Lys Pro Leu Glu Asp Lys Ile Leu Val Gln Ile Asn Glu Ala Glu Thr Thr Ala Ser Gly Leu Val Ile Pro Asp 20 Ser Ala Lys Glu Lys Pro Gln Glu Ala Thr Val Ile Ala Val Gly Pro 40 Gly Arg Phe Asp Asp Lys Gly Asn Arg Ile Pro Leu Asp Ile Lys Glu Asp Asp Val Val Ile Phe Ser Arg Tyr Gly Gly Thr Glu Ile Lys Phe Gly Gly Val Glu Tyr Leu Leu Ser Ala Arg Asp Ile Leu Ala Ile 85 Val Glu Lys <210> 5 <211> 1737 <212> DNA <213> Corynebacterium glutamicum <220> <221> CDS <222> (101)..(1714) <223> RXN00493 cccqttacqq cqqcaccqaq atcaaqttcq gtqqcqtqqa gtacttqctt ctctccqctc 60 qtqacatcct cqcaatcqtc qaqaaqtaqq qqataaqttc atq qca aaq ctc att Met Ala Lys Leu Ile 1

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163

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_			-	-	ctt Leu	-			-	-	-	•	-		-	1507
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165 170 175

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- Ile Thr Val Ser Lys Asp Glu Thr Ile Ile Val Asp Gly Ala Gly Ser 325 330 335
- Ala Glu Asp Val Glu Ala Arg Arg Gly Gln Ile Arg Arg Glu Ile Ala 340 345 350
- Asn Thr Asp Ser Thr Trp Asp Arg Glu Lys Ala Glu Glu Arg Leu Ala 355 360 365
- Lys Leu Ser Gly Gly Ile Ala Val Ile Arg Val Gly Ala Ala Thr Glu 370 375 380
- Thr Glu Val Asn Asp Arg Lys Leu Arg Val Glu Asp Ala Ile Asn Ala 385 390 395 400
- Ala Arg Ala Ala Gl
n Glu Gly Val Ile Ala Gly Gly Gly Ser Ala 405 410 415
- Leu Val Gln Ile Ala Glu Thr Leu Lys Ala Tyr Ala Glu Glu Phe Glu 420 425 430
- Gly Asp Gln Lys Val Gly Val Arg Ala Leu Ala Thr Ala Leu Gly Lys 435 440 445
- Pro Ala Tyr Trp Ile Ala Ser Asn Ala Gly Leu Asp Gly Ser Val Val 450 455 460
- Val Ala Arg Thr Ala Ala Leu Pro Asn Gly Glu Gly Phe Asn Ala Ala

470 475 465 480 Thr Leu Glu Tyr Gly Asn Leu Ile Asn Asp Gly Val Ile Asp Pro Val 485 490 Lys Val Thr His Ser Ala Val Val Asn Ala Thr Ser Val Ala Arg Met 505 Val Leu Thr Thr Glu Ala Ser Val Val Glu Lys Pro Ala Glu Glu Ala 520 Ala Asp Ala His Ala Gly His His His 535 <210> 7 <211> 1339 <212> DNA <213> Corynebacterium glutamicum <220> <221> CDS <222> (101)..(1339) <223> FRXA00498 cccgttacgg cggcaccgag atcaagttcg gtggcgtgga gtacttgctt ctctccgctc 60 gtgacatcct cgcaatcgtc gagaagtagg ggataagttc atg gca aag ctc att Met Ala Lys Leu Ile get ttt gac cag gac gec ege gaa ggc att etc egg gge gtt gac get . 163Ala Phe Asp Gln Asp Ala Arg Glu Gly Ile Leu Arg Gly Val Asp Ala 10 ctg gca aac gct gtc aag gta acc ctc ggc cca cgc ggc cgt aac gtg 211 Leu Ala Asn Ala Val Lys Val Thr Leu Gly Pro Arg Gly Arg Asn Val 25 gtt ctt gat aag gca ttc ggc gga cct ctg gtc acc aac gac ggt gtc 259 Val Leu Asp Lys Ala Phe Gly Gly Pro Leu Val Thr Asn Asp Gly Val 40 45 50 acc att gcc cgc gac atc gac ctt gag gat cct ttt gag aac ctc ggt 307 Thr Ile Ala Arg Asp Ile Asp Leu Glu Asp Pro Phe Glu Asn Leu Gly 55 gcg cag ctg gtg aag tcc gtt gct gtt aag acc aac gac atc gct ggt Ala Gln Leu Val Lys Ser Val Ala Val Lys Thr Asn Asp Ile Ala Gly 70 75 gac ggc acc acg act gca act ctg ctt qct caq qca ctc att qct qaa Asp Gly Thr Thr Thr Ala Thr Leu Leu Ala Gln Ala Leu Ile Ala Glu 90 95 100 ggc ctg cgc aac gtt gct gcc gca aac cca atg gag ctc aac aag

Gly	Leu	Arg	Asn 105		Ala	Ala	Gly	Ala 110		Pro	Met	Glu	Leu 115		Lys	
			Ala					Thr			gag Glu		Lys			499
		Glu					Lys				aac Asn 145					547
	Ser										gct Ala					595
					Gly						gag Glu					643
											ttc Phe					691
											cag Gln					739
											att Ile 225					787
_				_	_		-	_			tcc Ser		_		_	835
-			_	-	-	-					ttg Leu	-		_	gtt Val	883
				_	-			-	-	-	gca Ala		_			931
											gac Asp					979
											atc Ile 305					1027
											atc Ile					1075
											gca Ala					1123

att gct gtc atc cgc gtt ggt gca gca act gaa acc gaa gtc aac gac 1267 Ile Ala Val Ile Arg Val Gly Ala Ala Thr Glu Thr Glu Val Asn Asp 375 380 385

cgc aag ctg cgt gtc gaa gat gcc atc aac gct gct cgc gca gca gca 1315 Arg Lys Leu Arg Val Glu Asp Ala Ile Asn Ala Ala Arg Ala Ala Ala 390 395 400 405

caa gaa ggc gtt atc gct ggc 1339 Gln Glu Gly Val Ile Ala Gly Gly 410

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<213> Corynebacterium glutamicum

<400> 8

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Arg Gly Arg Asn Val Val Leu Asp Lys Ala Phe Gly Gly Pro Leu Val
35 40 45

Thr Asn Asp Gly Val Thr Ile Ala Arg Asp Ile Asp Leu Glu Asp Pro 50 55

Phe Glu Asn Leu Gly Ala Gln Leu Val Lys Ser Val Ala Val Lys Thr 65 70 75 80

Asn Asp Ile Ala Gly Asp Gly Thr Thr Thr Ala Thr Leu Leu Ala Gln
85 90 95

Ala Leu Ile Ala Glu Gly Leu Arg Asn Val Ala Ala Gly Ala Asn Pro 100 105 110

Met Glu Leu Asn Lys Gly Ile Ser Ala Ala Ala Glu Lys Thr Leu Glu 115 120 125

Glu Leu Lys Ala Arg Ala Thr Glu Val Ser Asp Thr Lys Glu Ile Ala 130 135 140

Asn Val Ala Thr Val Ser Ser Arg Asp Glu Val Val Gly Glu Ile Val

150 155 145 Ala Ala Met Glu Lys Val Gly Lys Asp Gly Val Val Thr Val Glu 170 Glu Ser Gln Ser Ile Glu Thr Ala Leu Glu Val Thr Glu Gly Ile Ser 185 Phe Asp Lys Gly Tyr Leu Ser Pro Tyr Phe Ile Asn Asp Asn Asp Thr 200 Gln Gln Ala Val Leu Asp Asn Pro Ala Val Leu Leu Val Arg Asn Lys 215 Ile Ser Ser Leu Pro Asp Phe Leu Pro Leu Leu Glu Lys Val Val Glu 235 230 225 Ser Asn Arg Pro Leu Leu Ile Ile Ala Glu Asp Val Glu Glu Pro Leu Gln Thr Leu Val Val Asn Ser Ile Arg Lys Thr Ile Lys Val Val Ala Val Lys Ser Pro Tyr Phe Gly Asp Arg Lys Ala Phe Met Asp 280 Asp Leu Ala Ile Val Thr Lys Ala Thr Val Val Asp Pro Glu Val Gly Ile Asn Leu Asn Glu Ala Gly Glu Glu Val Phe Gly Thr Ala Arg Arg Ile Thr Val Ser Lys Asp Glu Thr Ile Ile Val Asp Gly Ala Gly Ser 330 Ala Glu Asp Val Glu Ala Arg Arg Gly Gln Ile Arg Arg Glu Ile Ala 345 Asn Thr Asp Ser Thr Trp Asp Arg Glu Lys Ala Glu Glu Arg Leu Ala Lys Leu Ser Gly Gly Ile Ala Val Ile Arg Val Gly Ala Ala Thr Glu Thr Glu Val Asn Asp Arg Lys Leu Arg Val Glu Asp Ala Ile Asn Ala Ala Arg Ala Ala Gln Glu Gly Val Ile Ala Gly Gly

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acc ctg gtt gag gat cct gag acc ctc atc gtc aac atc gtt ctc cca

Thr Leu Val Glu Asp Pro Glu Thr Leu Ile Val Asn Ile Val Leu Pro

get gte gag gaa gaa gac ace gaa gag gac gaa get gaa gaa gea

Ala Val Glu Glu Glu Asp Thr Glu Glu Asp Glu Ala Ala Glu Glu Ala

175

170

643

691.

185 190 195

gct act gag taagcttttt tagatagctt tat Ala Thr Glu 200 723

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<211> 200

<212> PRT

<213> Corynebacterium glutamicum

<400> 10

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Val Tyr Gly Ala Asp Val Glu Ser Asn Leu His Val Thr Ile Asp His 35 40 45

Arg Thr Phe Ala Ala Leu Val Arg Gln Glu Gly Val Asn Ala Val Leu 50 55 60

Glu Leu Asp Ile Glu Gly Gln Lys Gln Leu Thr Met Ile Lys His Ile 65 70 75 80

Asp Gln Asn Val Leu Thr Phe His Ile Asp His Leu Asp Leu Leu Ala 85 90 95

Ile Lys Arg Gly Glu Lys Val Glu Val Asp Val Pro Val Ile Val Glu 100 105 110

Gly Glu Pro Ala Pro Gly Thr Met Trp Val Gln Asp Ala Asp Thr Ile 115 120 125

Lys Val Glu Ala Asp Val Leu Ser Ile Pro Glu Glu Phe Thr Val Ser 130 135 140

Ile Glu Gly Leu Glu Leu Gly Ala Gln Ile Thr Ala Ala Asp Ile Lys 145 150 155 160

Leu Glu Gly Asp Thr Thr Leu Val Glu Asp Pro Glu Thr Leu Ile Val 165 170 175

Asn Ile Val Leu Pro Ala Val Glu Glu Glu Asp Thr Glu Glu Asp Glu 180 185 190

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<210> 11

<211> 1603

<212> DNA

<213> Corynebacterium glutamicum

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185 190 195

acc Thr 200	cct Pro	aag Lys	acc Thr	tcc Ser	cgc Arg 205	cac His	cag Gln	gac Asp	ggc Gly	ttc Phe 210	ggc Gly	tcc Ser	cac His	acc Thr	ttc Phe 215	677
cag Gln	tgg Trp	atc Ile	aac Asn	gct Ala 220	gaa Glu	ggt Gly	aag Lys	cca Pro	gtt Val 225	tgg Trp	gtt Val	aag Lys	tac Tyr	cac His 230	ttc Phe	725
					tgg Trp											773
					gct Ala											821
att Ile	gaa Glu 265	aac Asn	ggc Gly	gac Asp	ttc Phe	cca Pro 270	atc Ile	tgg Trp	gac Asp	gtc Val	aag Lys 275	gtt Val	cag Gln	atc Ile	atg Met	869
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															ttc Phe	965
					cca Pro											1013
					aac Asn											1061
					cgt Arg											1109
					tac Tyr 365											1157
					agc Ser											1205
					tcc Ser											1253
					ggt Gly											1301

		Ala			atc Ile											1349
	Val				tac Tyr 445											1397
_					tac Tyr	-		-	_	-				_		1445
					atc Ile											1493
					tac Tyr											1541
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tgai	tttaa	aaa t	ga													1603
	0> 12 l> 53															
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Leu Arg Phe Tyr Thr Glu Glu Gly Asn Tyr Asp Ile Val Gly Asn Asn 130 135 140

- Thr Pro Thr Phe Phe Leu Arg Asp Gly Met Lys Phe Pro Asp Phe Ile 145 150 155 160
- His Ser Gln Lys Arg Leu Asn Lys Asn Gly Leu Arg Asp Ala Asp Met
 165 170 175
- Gln Trp Asp Phe Trp Thr Arg Ala Pro Glu Ser Ala His Gln Val Thr 180 185 190
- Tyr Leu Met Gly Asp Arg Gly Thr Pro Lys Thr Ser Arg His Gln Asp 195 200 205
- Gly Phe Gly Ser His Thr Phe Gln Trp Ile Asn Ala Glu Gly Lys Pro 210 215 220
- Val Trp Val Lys Tyr His Phe Lys Thr Arg Gln Gly Trp Asp Cys Phe 225 230 235 240
- Thr Asp Ala Glu Ala Ala Lys Val Ala Gly Glu Asn Ala Asp Tyr Gln 245 250 255
- Arg Glu Asp Leu Tyr Asn Ala Ile Glu Asn Gly Asp Phe Pro Ile Trp 260 265 270
- Asp Val Lys Val Gln Ile Met Pro Phe Glu Asp Ala Glu Asn Tyr Arg 275 280 285
- Trp Asn Pro Phe Asp Leu Thr Lys Thr Trp Ser Gln Lys Asp Tyr Pro 290 295 300
- Leu Ile Pro Val Gly Tyr Phe Ile Leu Asn Arg Asn Pro Arg Asn Phe 305 310 315 320
- Phe Ala Gln Ile Glu Gln Leu Ala Leu Asp Pro Gly Asn Ile Val Pro 325 330 335
- Gly Val Gly Leu Ser Pro Asp Arg Met Leu Gln Ala Arg Ile Phe Ala 340 345 350
- Tyr Ala Asp Gln Gln Arg Tyr Arg Ile Gly Ala Asn Tyr Arg Asp Leu 355 360 365
- Pro Val Asn Arg Pro Ile Asn Glu Val Asn Thr Tyr Ser Arg Glu Gly 370 375 380
- Ser Met Gln Tyr Ile Phe Asp Ala Glu Gly Glu Pro Ser Tyr Ser Pro 385 390 395 400
- Asn Arg Tyr Asp Lys Gly Ala Gly Tyr Leu Asp Asn Gly Thr Asp Ser 405 410 415
- Ser Ser Asn His Thr Ser Tyr Gly Gln Ala Asp Asp Ile Tyr Val Asn 420 425 430

Pro Asp Pro His Gly Thr Asp Leu Val Arg Ala Ala Tyr Val Lys His Gln Asp Asp Asp Phe Ile Gln Pro Gly Ile Leu Tyr Arg Glu Val 455 Leu Asp Glu Gly Glu Lys Glu Arg Leu Ala Asp Asn Ile Ser Asn Ala 475 Met Gln Gly Ile Ser Glu Ala Thr Glu Pro Arg Val Tyr Asp Tyr Trp 485 490 Asn Asn Val Asp Glu Asn Leu Gly Ala Arg Val Lys Glu Leu Tyr Leu. Gln Lys Lys Ala 515 <210> 13 <211> 2439 <212> DNA <213> Corynebacterium glutamicum <220> <221> CDS <222> (101)..(2416) <223> RXA00404 <400> 13 aagatccgat catcggcata cagaaacacc catctggccg aactttcctt tttctgcatg 60 catttctgca cacagtttct gcccgctgtt tctacgcata gtg gct ttg aaa cga 115 Val Ala Leu Lys Arg ccc gaa gag aaa aca gta aag atc gtg acc ata aaa cag act gac aac 163 Pro Glu Glu Lys Thr Val Lys Ile Val Thr Ile Lys Gln Thr Asp Asn 10 15 atc aat gac gat gat ttg gtg tac agc aac gct act gac ctt cca gta 211 Ile Asn Asp Asp Asp Leu Val Tyr Ser Asn Ala Thr Asp Leu Pro Val 30 ggc gtg aag aag too cot aaa atg toa cog acc goo logo gtt ggt oto 259 Gly Val Lys Lys Ser Pro Lys Met Ser Pro Thr Ala Arg Val Gly Leu ctt gtc ttt ggg gtt atc gcg gcg gtg ggt tgg gga gca atc gct ttc 307 Leu Val Phe Gly Val Ile Ala Ala Val Gly Trp Gly Ala Ile Ala Phe tcc cgt ggc gaa aca atc aac tct gtg tgg ctg gtt ttg gcg gca gtt Ser Arg Gly Glu Thr Ile Asn Ser Val Trp Leu Val Leu Ala Ala Val 75 80

					Ala			ttc Phe		Ala						403
				Pro				cga Arg 110	Ala							451
	_		Lys	_		-		acg Thr	-	-	_					499
								gcc Ala								547
-	-		_				_	cca Pro			_					595
				-		_		cag Gln	_				_			643
								ctt Leu 190								691
_		-	-			-	-	ggt Gly		-						739
-								gca Ala	_			-		-	-	787
-	-					-		tcc Ser			-					835
-	_		_	Gly	Val	Tyr	Leu	cgt Arg	Tyr	Leu	Arg	Pro	Gly	Arg	-	883
								gca Ala 270								931
								tca Ser								979
Trp								gcc Ala								1027
gct	gcg	att	ttg	ccg	gtg	tgg	ctg	ctg	ctt	gca	ccg	cgc	gat	tac	ctg	1075

Ala 310		Ile	e Leu	Pro	Val 315		Leu	Leu	Leu	Ala 320		Arg	Asp	Tyr	Leu 325	
					atc Ile					Leu						1123
				Pro	gag Glu				Pro					Phe		1171
			Asn		ccg Pro					_	_				_	1219
		Thr			tgt Cys											1267
					cca Pro 395	_		, ,		_	-		_	-	_	1315
_					ggc Gly	_	_	_	_					_	-	1363
					gtt Val											1411
					ctg Leu											1459
	-				ggg Gly	_				-			_	_	-	1507
_	-	_	-		gaa Glu 475	-	-		-			-			_	1555
					acc Thr											1603
					gct Ala											1651
					ctg Leu	Phe										1699
					atg Met											1747

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ttg gag acc act gaa gag cct gat act gaa tct gag ttc ttc gcc cca 2323 Leu Glu Thr Thr Glu Glu Pro Asp Thr Glu Ser Glu Phe Phe Ala Pro 730

act gga ttc ctt gca tct tcc agg gat aag gaa gtc cag gcc atg tgg Thr Gly Phe Leu Ala Ser Ser Arg Asp Lys Glu Val Gln Ala Met Trp 745

qac qaq cqc tac cca qgc qqt qcq ccc qtq tct tct qqa qqq cac 2416 Asp Glu Arg Tyr Pro Gly Gly Ala Pro Val Ser Ser Gly Gly His 760 765

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2439

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<211> 772

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<400> 14

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Thr Asp Leu Pro Val Gly Val Lys Lys Ser Pro Lys Met Ser Pro Thr 35 40 45

Ala Arg Val Gly Leu Leu Val Phe Gly Val Ile Ala Ala Val Gly Trp 50 55 60

Gly Ala Ile Ala Phe Ser Arg Gly Glu Thr Ile Asn Ser Val Trp Leu 65 70 75 80

Val Leu Ala Ala Val Gly Ser Tyr Ile Ile Ala Phe Ser Phe Tyr Ala 85 90 95

Arg Leu Ile Glu Tyr Lys Val Val Lys Pro Lys Asp Gln Arg Ala Thr 100 105 110

Pro Ala Glu Tyr Val Asn Asp Gly Lys Asp Tyr Val Pro Thr Asp Arg 115 120 125

Arg Val Leu Phe Gly His His Phe Ala Ala Ile Ala Gly Ala Gly Pro 130 135 140

Leu Val Gly Pro Val Met Ala Ala Gln Met Gly Tyr Leu Pro Gly Thr 145 150 155 160

Leu Trp Ile Ile Leu Gly Val Ile Phe Ala Gly Ala Val Gln Asp Tyr 165 170 175

Leu Val Leu Trp Val Ser Thr Arg Arg Gly Arg Ser Leu Gly Gln 180 185 190

Met Val Arg Asp Glu Met Gly Thr Val Gly Gly Ala Ala Gly Ile Leu 195 200 205

Ala Thr Ile Ser Ile Met Ile Ile Ile Ile Ala Val Leu Ala Leu Ile 210 215 220

Val Val Asn Ala Leu Ala Asp Ser Pro Trp Gly Val Phe Ser Ile Thr 225 230 235 240

Met Thr Ile Pro Ile Ala Leu Phe Met Gly Val Tyr Leu Arg Tyr Leu 245 250 255

- Arg Pro Gly Arg Val Thr Glu Val Ser Ile Ile Gly Val Ala Leu Leu 260 265 270
- Leu Leu Ala Ile Val Ala Gly Gly Trp Val Ala Asp Thr Ser Trp Gly 275 280 285
- Val Glu Trp Phe Thr Trp Ser Lys Thr Thr Leu Ala Leu Ala Leu Ile 290 295 300
- Gly Tyr Gly Ile Met Ala Ala Ile Leu Pro Val Trp Leu Leu Leu Ala 305 310 315 320
- Pro Arg Asp Tyr Leu Ser Thr Phe Met Lys Ile Gly Val Ile Gly Leu 325 330 335
- Leu Ala Val Gly Ile Leu Phe Ala Arg Pro Glu Val Gln Met Pro Ser 340 345 350
- Val Thr Ser Phe Ala Leu Glu Gly Asn Gly Pro Val Phe Ser Gly Ser 355 360 365
- Leu Phe Pro Phe Leu Phe Ile Thr Ile Ala Cys Gly Ala Leu Ser Gly 370 375 380
- Phe His Ala Leu Ile Ser Ser Gly Thr Thr Pro Lys Leu Val Glu Lys 385 390 395 400
- Glu Ser Gln Met Arg Met Leu Gly Tyr Gly Gly Met Leu Met Glu Ser 405 410 415
- Phe Val Ala Met Met Ala Leu Ile Thr Ala Val Ile Leu Asp Arg His 420 425 430
- Leu Tyr Phe Ser Met Asn Ala Pro Leu Ala Leu Thr Gly Gly Asp Pro 435 440 445
- Ala Thr Ala Ala Glu Trp Val Asn Ser Ile Gly Leu Thr Gly Ala Asp 450 455 460
- Ile Thr Pro Glu Gln Leu Ser Glu Ala Ala Glu Ser Val Gly Glu Ser465470475480
- Thr Val Ile Ser Arg Thr Gly Gly Ala Pro Thr Leu Ala Phe Gly Met 485 490 495
- Ser Glu Ile Leu Ser Gly Phe Ile Gly Gly Ala Gly Met Lys Ala Phe 500 510
- Trp Tyr His Phe Ala Ile Met Phe Glu Ala Leu Phe Ile Leu Thr Thr 515 520 525
- Val Asp Ala Gly Thr Arg Val Ala Arg Phe Met Met Thr Asp Thr Leu 530 535 540
- Gly Asn Val Pro Gly Leu Arg Arg Phe Lys Asp Pro Ser Trp Thr Val 545 550 555 560

Gly Asn Trp Ile Ser Thr Val Phe Val Cys Ala Leu Trp Gly Ala Ile 565 570 575

Leu Leu Met Gly Val Thr Asp Pro Leu Gly Gly Ile Asn Val Leu Phe 580 585 590

Pro Leu Phe Gly Ile Ala Asn Gln Leu Leu Ala Ala Ile Ala Leu Ala 595 600 605

Leu Val Leu Val Val Val Lys Lys Gly Leu Tyr Lys Trp Ala Trp 610 615 620

Ile Pro Ala Val Pro Leu Ala Trp Asp Leu Ile Val Thr Met Thr Ala 625 630 635 640

Ser Trp Gln Lys Ile Phe His Ser Asp Pro Ala Ile Gly Tyr Trp Ala 645 650 655

Gln Asn Ala Asn Phe Arg Asp Ala Lys Ser Gln Gly Leu Thr Glu Phe 660 665 670

Gly Ala Ala Lys Ser Pro Glu Ala Ile Asp Ala Val Ile Arg Asn Thr 675 680 685

Met Ile Gln Gly Ile Leu Ser Ile Leu Phe Ala Val Leu Val Leu Val 690 695 700

Val Val Gly Ala Ala Ile Ala Val Cys Ile Lys Ser Ile Arg Ala Arg 705 710 715 720

Ala Ala Gly Thr Pro Leu Glu Thr Thr Glu Glu Pro Asp Thr Glu Ser 725 730 735

Glu Phe Phe Ala Pro Thr Gly Phe Leu Ala Ser Ser Arg Asp Lys Glu 740 745 750

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Ser Gly Gly His 770

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gct gaa atc atg gag ctt gac cag tcc aag gac cac gca acc tac gtt Ala Glu Ile Met Glu Leu Asp Gln Ser Lys Asp His Ala Thr Tyr Val 25 30 35	211
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gag cac gct ttc tac ctg cag tac atg aac gtt aag gca gat tac gtc Glu His Ala Phe Tyr Leu Gln Tyr Met Asn Val Lys Ala Asp Tyr Val 10 15 20	163
aag gct gtt tgg aac gtc ttc aac tgg gac gac gca aga gca cgc ttc Lys Ala Val Trp Asn Val Phe Asn Trp Asp Asp Ala Arg Ala Arg Phe 25 30 35	211

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70 75 80 403 gat tee ate tat ate cae eee cag gge caa gge ega gga ate gge gge Asp Ser Ile Tyr Ile His Pro Gln Gly Gln Gly Arg Gly Ile Gly Gly gct ttg ctc gac gcc ctt atc acc tac tgc gaa agc aac ggc atc tgg 451 Ala Leu Leu Asp Ala Leu Ile Thr Tyr Cys Glu Ser Asn Gly Ile Trp 110 499 teg ate cae tee tgg ate tte eeg gaa aac ete ggt tet geg aaa etg Ser Ile His Ser Trp Ile Phe Pro Glu Asn Leu Gly Ser Ala Lys Leu cat gaa tog aag ggc ttc gtg aag gtg ggc acc atg cac caa atg gca 547 His Glu Ser Lys Gly Phe Val Lys Val Gly Thr Met His Gln Met Ala 140 595 agg atg ccc tac ggc gag atg gaa gga caa tgg cgc gat tgt gat ctg Arg Met Pro Tyr Gly Glu Met Glu Gly Gln Trp Arg Asp Cys Asp Leu 155 tgg gag tgc ctc tta tcc gtt cca gag caa gct caa agt tcc 637 Trp Glu Cys Leu Leu Ser Val Pro Glu Gln Ala Gln Ser Ser 660 taaagcaatt taaatctgac ttt <210> 20 <211> 179 <212> PRT <213> Corynebacterium glutamicum Met Val Glu Arg Asp Phe Thr Ile Arg Pro Ile Arg Glu Gly Asp Phe Pro Gln Val Arg Asp Ile Tyr Glu Leu Gly Leu Glu Thr Gly His Ala Thr Tyr Glu Thr Ser Gly Pro Thr Trp Asp Gln Phe Ser Gln Ser Lys Ile Met Asp Thr Val Met Val Ala Val Glu Asn Asn Asp Pro Asp Phe Ile Leu Gly Trp Val Ser Ala Ala Pro Ile Ser Ser Arg Gln Val Phe 70 His Gly Val Val Glu Asp Ser Ile Tyr Ile His Pro Gln Gly Gln Gly Arg Gly Ile Gly Gly Ala Leu Leu Asp Ala Leu Ile Thr Tyr Cys Glu 100 105 110 Ser Asn Gly Ile Trp Ser Ile His Ser Trp Ile Phe Pro Glu Asn Leu

PCT/IB00/00922

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gct cca att tca agc cga cag gtt ttc cat gga gtg gtg gaa gat tcc Ala Pro Ile Ser Ser Arg Gln Val Phe His Gly Val Val Glu Asp Ser - 55 ate tat ate cae ece cag gge caa gge ega gga ate gge gge get ttg 355 Ile Tyr Ile His Pro Gln Gly Gln Gly Arg Gly Ile Gly Gly Ala Leu 70 75 80

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cac tcc tgg atc ttc ccg gaa aac ctc ggt tct gcg aaa ctg cat gaa 451

His	s Sei	r Trj	10:		e Pro	o Glu	ı Ası	n Lei 110	_	y Sei	Ala	Lys	115		Glu	
			/ Phe					y Thi					Ala		atg Met	
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Glu	Thr	Ser	Gly 20		Thr	Trp	Asp	Gln 25		Ser	Gln	Ser	Lys 30	Ile	Met	
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.Gly	Trp 50	Val	Ser	Ala	Ala	Pro 55	Ile	Ser	Ser	Arg	Gln 60	Val	Phe	His	Gly	
Val 65	Val	Glu	Asp	Ser	Ile 70	Tyr	Ile	His	Pro	Gln 75	Gly	Gln	Gly	Arg	Gly 80	
Ile	Gly	Gly	Ala	Leu 85	Leu	Asp	Ala	Leu	Ile 90	Thr	Tyr	Cys	Glu	Ser 95	Asn	
Gly			Ser 100					Ile 105							Ser	
Ala	Lys	Leu 115	His	Glu	Ser	Lys	Gly 120	Phe	Val	Lys	Val	Gly 125	Thr	Met	His	
Gln	Met 130	Ala	Arg	Met	Pro	Tyr 135	Gly	Glu	Met	Glu	Gly 140	Gln	Trp	Arg	Asp	
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Ser

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			Val											ggt Gly		259
		Ile					Asp							tct Ser		307
	_				_			_	_	-	-		-	gtc Val		355
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														cac His		499
														atc Ile		547
														tac Tyr		595

					acc Thr											643
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					ggc Gly											931
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					ggt Gly	-	-				_					1171
					cgc Arg											1219
	-			-	gcc Ala		_		-	_	-			_	-	1267

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att tcc atc aag ata ctc ggc ggc gtt acc gtc gag cac aca att Ile Ser Ile Lys Ile Leu Gly Gly Val Thr Val Glu His Thr Ile 470 475 480	1552
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- Ala Phe Glu Tyr Thr His Arg His Ala Arg Thr Leu Asn Ser Lys Arg 165 170 175
- Gln Ala Ile Val Val Tyr Asp Leu Gly Gly Gly Thr Phe Asp Ser Ser 180 185 190
- Leu Ile Arg Ile Asp Gly Thr His His Glu Val Val Ser Ser Ile Gly
 195 200 205
- Ile Ser Arg Leu Gly Gly Asp Asp Phe Asp Glu Ile Leu Leu Gln Cys 210 215 220
- Ala Leu Lys Ala Ala Gly Arg Gln His Asp Ala Phe Gly Lys Arg Ala 225 230 235 240
- Lys Asn Thr Leu Leu Asp Glu Ser Arg Asn Ala Lys Glu Ala Leu Val 245 250 255
- Pro Gln Ser Arg Arg Leu Val Leu Glu Ile Gly Asp Asp Ile Thr 260 265 270
- Val Pro Val Asn Lys Phe Tyr Glu Ala Ala Thr Pro Leu Val Glu Lys 275 280 285
- Ser Leu Ser Ile Met Glu Pro Leu Ile Gly Val Asp Asp Leu Lys Asp 290 295 300
- Ser Asp Ile Ala Gly Ile Tyr Leu Val Gly Gly Gly Ser Ser Leu Pro 305 310 315 320
- Leu Val Ser Arg Leu Leu Arg Glu Arg Phe Gly Arg Arg Val His Arg 325 330 335
- Ser Pro Phe Pro Ser Gly Ser Thr Ala Val Gly Leu Ala Ile Ala Ala 340 . 345 350
- Asp Pro Ser Ser Gly Phe His Leu Arg Asp Arg Val Ala Arg Gly Ile 355 360 365
- Gly Val Phe Arg Glu His Asp Ser Gly Arg Ala Val Ser Phe Asp Pro 370 375 380
- Leu Ile Ala Pro Asp Thr Asp Ser Ala Thr Val Ala Lys Arg Cys Tyr 385 390 395 400
- Lys Ala Val His Asn Ile Gly Trp Phe Arg Phe Val Glu Tyr Ser Thr 405 410 415
- Val Ser Glu Asp Gly Ser Pro Gly Asp Ile Ser Leu Leu Ser Glu Ile 420 425 430

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		Arc		cto Leu			Ser					Thr				547
-	Val		-	gto Val		Glu		-	-	_	Āla					595
				cgc Arg 170	Thr					Arg						643
	-	-		ggc Gly				_		-			-		_	691
			His	gag Glu	_								-			739
				gat Asp												787
	_	-		gat Asp				_	_	_			_			835
Asp	Glu	Ser	Arg	aac Asn 250	Ala	Lys	Glu	Ala	Leu 255	Val	Pro	Gln	Ser	Arg 260	Arg	883
				att Ile												931
				gcc Ala												979
-				ggc Gly	_	-	_			-		_		-		1027
				ggt Gly												1075
			Arg	ttc Phe 330												1123

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Phe Val Arg Ser Phe Lys Arg Leu Leu Ser Glu Pro Asn Val Thr Glu 65 70 75 80

Ala Thr Pro Val Tyr Leu Gly Asp His Val His Pro Leu Gly Ala Val 85 90 95

Leu Glu Ala Phe Ala Glu Asn Val Val Thr Ala Leu Arg Ala Phe Gln 100 105 110

Thr Gln Leu Gly Asp Thr Ser Pro Ile Glu Val Val Ile Gly Val Pro 115 120 125

Ala Asn Ser His Ser Ala Gln Arg Leu Leu Thr Met Ser Ala Phe Ser 130 135 140

Ala Thr Gly Ile Thr Val Val Gly Leu Val Asn Glu Pro Ser Ala Ala 145 150 155 160

Ala Phe Glu Tyr Thr His Arg His Ala Arg Thr Leu Asn Ser Lys Arg 165 170 175

Gln Ala Ile Val Val Tyr Asp Leu Gly Gly Gly Thr Phe Asp Ser Ser 180 185 190

Leu Ile Arg Ile Asp Gly Thr His His Glu Val Val Ser Ser Ile Gly 195 200 205

39

Ile Ser Arg Leu Gly Gly Asp Asp Phe Asp Glu Ile Leu Leu Gln Cys 215 Ala Leu Lys Ala Ala Gly Arg Gln His Asp Ala Phe Gly Lys Arg Ala 225 230 235 Lys Asn Thr Leu Leu Asp Glu Ser Arg Asn Ala Lys Glu Ala Leu Val Pro Gln Ser Arg Arg Leu Val Leu Glu Ile Gly Asp Asp Asp Ile Thr Val Pro Val Asn Lys Phe Tyr Glu Ala Ala Thr Pro Leu Val Glu Lys 280 Ser Leu Ser Ile Met Glu Pro Leu Ile Gly Val Asp Asp Leu Lys Asp Ser Asp Ile Ala Gly Ile Tyr Leu Val Gly Gly Ser Ser Leu Pro Leu Val Ser Arg Leu Leu Arg Glu Arg Phe Gly Arg Arg Val His Arg 325 Ser Pro Phe Pro Ser Gly Ser Thr Ala Val Gly Leu Ala Ile Ala Ala Asp Pro Ser Ser Gly Phe His Leu Arg Asp Arg Val Ala Arg Gly Ile 360 355 Gly Val Phe Arg Glu His Asp Ser Gly Arg Ala Val Ser Phe Asp Pro Leu Ile Ala Pro Asp 385 <210> 27 <211> 1308 <212> DNA <213> Corynebacterium glutamicum <220> <221> CDS <222> (101)..(1285) <223> RXA02541 <400> 27 atcogcoggt gtccggacaa caaaacttgc aacacaagat aacttaagaa attgcataca 60 attcaccgca tataagactc atggaaggag gggatgccca gtg aac aac agc gaa Val Asn Asn Ser Glu tgg gca aat aag aac tat tac gca gac ctg ggg gtc tcc tcg tcc gct Trp Ala Asn Lys Asn Tyr Tyr Ala Asp Leu Gly Val Ser Ser Ser Ala

10 15 20

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										gat Asp					307
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_				-			_			gga Gly	 				451
										atc Ile					499
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										cgg Arg 240					835

					act Thr											883
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Leu	Ala	Arg 35	Glu .	Asn	His	Pro	Asp 40	Lys	Asn	Pro	Gly	Asp 45	Lys	Ala	Ala	

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- Gly Phe Arg Thr Ser Thr Gly Gly Phe Asp Thr Ser Asp Leu Phe Gly
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- Gly Gly Gln Gly Gly Phe Ser Thr Asp Gly Gly Leu Gly Asp Ile 115 120 125
- Phe Gly Gly Leu Phe Asn Arg Gly Ala Gly Ser His Gln Ser Ala Arg 130 135 140
- Pro Thr Arg Gly Ala Asp Val Gln Thr Glu Ile Thr Leu Ser Phe Val 145 150 155 160
- Glu Ala Ala Lys Gly Thr Thr Ile Pro Val Glu Leu Thr Gly Asp Ala 165 170 175
- Pro Cys Asn Thr Cys His Gly Ser Gly Ser Lys Ser Gly His Pro Ala 180 185 190
- Lys Cys Gly Thr Cys Asp Gly Thr Gly Phe Thr Ser Glu Asn Lys Gly 195 200 205
- Ala Phe Gly Phe Ser Ala Pro Cys Ala Thr Cys Gly Gly Thr Gly Glu 210 215 220
- Ile Ile Thr Asp Pro Cys Asp Asn Cys His Gly Arg Gly Thr Val Arg 225 230 235 240
- Lys Ser Arg Ser Ile Thr Val Arg Ile Pro Thr Gly Val Glu Asp Gly 245 250 255
- Gln Lys Val Arg Leu Ala Gly Gln Gly Glu Ala Gly Pro Asn Gly Lys 260 265 270
- Pro Ala Gly Asp Leu Phe Val Lys Val His Val Lys Lys Asp Asp Val 275 280 285
- Phe Thr Arg Asp Gly Ser Asn Ile Leu Ile Thr Ile Pro Val Ser Phe 290 295 300
- Ser Glu Leu Ala Leu Gly Gly Ala Ile Ser Val Pro Thr Leu Asn Lys 305 310 315 320
- Pro Val Lys Leu Lys Leu Pro Ala Gly Thr Pro Asp Gly Arg Thr Leu 325 330 335
- Arg Val Arg Gly Arg Gly Ile Glu Ala Arg Asp Ser Thr Gly Asp Leu 340 345 350

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44

gca ggt gtt gtt acc caa ctt ctg ccg ttg ctc gac gat ctt gac ctg Ala Gly Val Val Thr Gln Leu Leu Pro Leu Leu Asp Asp Leu Asp Leu

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Glu Tyr Ala Asn Tyr Arg Arg Arg Thr Glu Arg Glu Arg Gln Gly Ile

Glu Thr Gln Leu Ala Glu Arg Thr Glu Asp Leu Gln Arg Val Thr Ala

Ile Asp Thr Ala Arg Ala Gly Val Val Thr Gln Leu Leu Pro Leu Leu 120

Asp Asp Leu Asp Leu Ala Glu Gln His Gly Asp Leu Asn Glu Gly Pro 130 135 Leu Lys Ser Leu Ser Asp Lys Leu Ile Asn Ile Leu Gly Gly Leu Lys 150 Val Glu Ser Phe Gly Glu Ile Gly Glu Ala Phe Asp Pro Glu Ile His 165 Glu Ala Val Gln Asp Leu Ser Gln Gly Asp Val Lys Val Leu Gly Thr 185 Val Leu Arg Lys Gly Tyr Arg Leu Gly Asp Arg Val Ile Arg Thr Ala 200 Met Val Leu Ile Gly Asp Pro Glu Glu Ser 210 215 <210> 31 <211> 1977 <212> DNA <213> Corynebacterium glutamicum <220> <221> CDS <222> (101)..(1954) <223> RXN02543 ctcaatgagg agtttttctt accggcgaaa gtcggtggga agcaagtcaa agctcaagcc 60 gtggacagta ctaaaatcac ctaaaacagg aggcaccatt atg gga cgt gca gta Met Gly Arg Ala Val gga att gac ctt gga acc acc aac tct gtg gtt tcc gta ctt gaa ggc 163 Gly Ile Asp Leu Gly Thr Thr Asn Ser Val Val Ser Val Leu Glu Gly 10 ggc gag cca gta gtt atc gca aac gca gaa ggc tca cgc acc acc cct 211 Gly Glu Pro Val Val Ile Ala Asn Ala Glu Gly Ser Arg Thr Thr Pro 25 30 tcc gtc gtt gca ttc gca aag aac ggt gaa gtt cta gtc ggc cag tcc 259 Ser Val Val Ala Phe Ala Lys Asn Gly Glu Val Leu Val Gly Gln Ser 40 45 get aag aac cag geg gte ace aac gtt gac ege ace att ege tee gte 307 Ala Lys Asn Gln Ala Val Thr Asn Val Asp Arg Thr Ile Arg Ser Val 55 aag cgc cac atc ggc acc gac tgg tcc gtt gct atc gat gac aag aac Lys Arg His Ile Gly Thr Asp Trp Ser Val Ala Ile Asp Asp Lys Asn 70 75 80 tac acc tea cag gaa atc teg get egt acc etg atg aag etg aag ege

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Туг	Thr	: Se	r Gli	n Gli 90	ı Ile	e Ser	Ala	a Arg	J Thi 95		ı Met	: Lys	Leu	Lys 100	-	
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-		-	а Туз		gag Glu	-		Gln	_	-			Lys	-	-	499
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					tcc Ser											787
					cgt Arg 235											835
					gca Ala											883
					ctg Leu											931
					cag Gln											979
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					ggt Gly											1075

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				gca Ala					Leu							1171
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				aag Lys												1267
				acc Thr	_	Arg							_	-	-	1315
				gtt Val 410	_		-	-		_			_	-		1363
_		-		aag Lys	_										-	1411
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_				gtc Val		-		_	_		_				-	1507
				acc Thr												1555
				atc Ile 490												1603
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				aag Lys												1699
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Ile Asp Asp Lys Asn Tyr Thr Ser Gln Glu Ile Ser Ala Arg Thr Leu 85 90 95	
Met Lys Leu Lys Arg Asp Ala Glu Ala Tyr Leu Gly Glu Asp Val Thr 100 105 110	
Asp Ala Val Ile Thr Val Pro Ala Tyr Phe Glu Asp Ser Gln Arg Gln 115 120 125	
Ala Thr Lys Glu Ala Gly Gln Ile Ala Gly Leu Asn Val Leu Arg Ile 130 135 140	
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- Thr Ser Gly Asp Asn Glu Leu Gly Gly Asp Asp Trp Asp Gln Arg Ile 195 200 205
- Val Asp Trp Leu Val Glu Lys Phe Gln Ser Ser Asn Gly Ile Asp Leu 210 215 220
- Thr Lys Asp Lys Met Ala Leu Gln Arg Leu Arg Glu Ala Ala Glu Lys 225 230 235 240
- Ala Lys Ile Glu Leu Ser Ser Gln Ser Ala Asn Ile Asn Leu Pro 245 250 255
- Tyr Ile Thr Val Asp Ala Asp Lys Asn Pro Leu Phe Leu Asp Glu Thr 260 265 270
- Leu Ser Arg Ala Glu Phe Gln Arg Ile Thr Gln Asp Leu Leu Ala Arg 275 280 285
- Thr Lys Thr Pro Phe Asn Gln Val Val Lys Asp Ala Gly Val Ser Val 290 295 300
- Ser Glu Ile Asp His Val Val Leu Val Gly Gly Ser Thr Arg Met Pro 305 310 315 320
- Ala Val Thr Glu Leu Val Lys Glu Leu Thr Gly Gly Arg Glu Pro Asn 325 330 335
- Lys Gly Val Asn Pro Asp Glu Val Val Ala Val Gly Ala Ala Leu Gln 340 345 350

3

- Ala Gly Val Leu Arg Gly Glu Val Lys Asp Val Leu Leu Leu Asp Val 355 360 365
- Thr Pro Leu Ser Leu Gly Ile Glu Thr Lys Gly Gly Val Met Thr Lys 370 375 380
- Leu Ile Glu Arg Asn Thr Thr Ile Pro Thr Lys Arg Ser Glu Thr Phe 385 390 395 400
- Thr Thr Ala Glu Asp Asn Gln Pro Ser Val Gln Ile Gln Val Phe Gln 405 410 415
- Gly Glu Arg Glu Ile Ala Thr Ala Asn Lys Leu Leu Gly Ser Phe Glu 420 425 430
- Leu Gly Gly Ile Ala Pro Ala Pro Arg Gly Val Pro Gln Ile Glu Val 435 440 445
- Thr Phe Asp Ile Asp Ala Asn Gly Ile Val His Val Thr Ala Lys Asp 450 455 460

Lys 465	GIY	Thr	GIY	ьуѕ	470		Thr	IIe	Thr	475		Asp	Gly	ser	480	
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Ala	Asp	Glu	Asp 500	Lys	Lys	Arg	Arg	Glu 505	Glu	Gln	Glu	Val	Arg 510		Asn	
Ala	Glu	Ser 515	Leu	Val	Tyr	Gln	Thr 520	Arg	Lys	Phe	Val	Glu 525	Glu	Asn	Ser	
Glu	Lys 530	Val	Ser	Glu	Asp	Leu 535	Lys	Ala	Lys	Val	Glu 540	Glu	Ala	Ala	Lys	
Gly 545	Val	Glu	Glu	Ala	Leu 550	Lys	Gly	Glu	Asp	Leu 555	Glu	Ala	Ile	Lys	Ala 560	
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Glu	Gly	Ala 595	Ala	Asp	Asp	Asn	Val 600	Val	Asp	Ala	Glu	Val 605	Val	Glu	Asp	
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									gtg Val 15							163
									gaa (Glu (211

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	_		_		-		aac Asn	_	_	_			-		-	307
	Arg					Asp	tgg Trp				Ile					355
			_	_	Ile	_	gct Ala	_		_	_	_	_	_	_	403
							gag Glu									451
							tca Ser 125									499
	-		-				gtt Val	-	-		-					547
							ctt Leu									595
	-	-		_			ggc Gly				_	_				643
			-		_	_	gag Glu	-	_	_				-		691
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							ggc Gly									787
							gca Ala									835
			_	-	_		atc Ile	Asn						-	_	883
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52

Ala	Asp	Lys	265) Le	ı Phe	e Leu	270		ı Thr	Let	ı Ser	275		Glu	
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	Val					/ Ser					Ala	gtt Val				1075
					Gly					Asn		ggt Gly				1123
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		-	Lys	-	_				_	-		cca Pro 370	_			1219
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												acc Thr				1315
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-		_		-	-							ggc Gly			-	1411
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495 500

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<212> PRT

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Leu Val Gly Gln Ser Ala Lys Asn Gln Ala Val Thr Asn Val Asp Arg

Thr Ile Arg Ser Val Lys Arg His Ile Gly Thr Asp Trp Ser Val Ala 70

Ile Asp Asp Lys Asn Tyr Thr Ser Gln Glu Ile Ser Ala Arg Thr Leu

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- Ala Thr Lys Glu Ala Gly Gln Ile Ala Gly Leu Asn Val Leu Arg Ile 130 135 140
- Val Asn Glu Pro Thr Ala Ala Ala Leu Ala Tyr Gly Leu Glu Lys Gly 145 150 155 160
- Glu Gln Glu Gln Thr Ile Leu Val Phe Asp Leu Gly Gly Gly Thr Phe 165 170 175
- Asp Val Ser Leu Leu Glu Ile Gly Asp Gly Val Val Glu Val Arg Ala 180 185 190
- Thr Ser Gly Asp Asn Glu Leu Gly Gly Asp Asp Trp Asp Gln Arg Ile 195 200 205
- Val Asp Trp Leu Val Glu Lys Phe Gln Ser Ser Asn Gly Ile Asp Leu 210 215 220
- Thr Lys Asp Lys Met Ala Leu Gln Arg Leu Arg Glu Ala Ala Glu Lys 225 230 235 240
- Ala Lys Ile Glu Leu Ser Ser Ser Gln Ser Ala Asn Ile Asn Leu Pro 245 250 255
- Tyr Ile Thr Val Asp Ala Asp Lys Asn Pro Leu Phe Leu Asp Glu Thr 260 265 270
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- Ser Glu Ile Asp His Val Val Leu Val Gly Gly Ser Thr Arg Met Pro 305 310 315 320
- Ala Val Thr Glu Leu Val Lys Glu Leu Thr Gly Gly Arg Glu Pro Asn 325 330 335
- Lys Gly Val Asn Pro Asp Glu Val Val Ala Val Gly Ala Ala Leu Gln 340 345 350
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385 390 395 400

Thr Thr Ala Glu Asp Asn Gln Pro Ser Val Gln Ile Gln Val Phe Gln 405 410 415

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Leu Gly Gly Ile Ala Pro Ala Pro Arg Gly Val Pro Gln Ile Glu Val 435 440 445

Thr Phe Asp Ile Asp Ala Asn Gly Ile Val His Val Thr Ala Lys Asp 450 455 460

Lys Gly Thr Gly Lys Glu Asn Thr Ile Thr Ile Gln Asp Gly Ser Gly 465 470 475 480

Leu Ser Gln Asp Glu Ile Asp Arg Met Ile Lys Asp Ala Glu Ala His
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Gly Val Glu Glu Ala Leu Lys Gly Glu Asp Leu Glu Ala Ile Lys Ala 545 550 555 560

Ala Val Glu Lys Leu Asn Thr Glu Ser Gln Glu Met Gly Lys Xaa Ile 565 570 575

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	Leu				cct Pro 235	Phe					Leu					835
					tat Tyr					Āla						883
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58

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- Lys Asp Arg Ala Thr Phe Ser Leu Val Asp Asn Gly Thr Gly Leu Thr 65 70 75 80
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- Arg Asp Glu Phe Gly Leu Gln Arg Glu Gly Arg Leu Gly Gln Phe Gly 100 105 110
- Ile Gly Leu Leu Ser Cys Phe Met Val Ala Asp Glu Ile Thr Met Val 115 120 125
- Ser His Ala Glu Gly Ala Ser Ala Ile Arg Trp Thr Gly His Ala Asp 130 135 140
- Gly Thr Phe Asn Leu Glu Ile Leu Gly Asp Asp Ala Thr Asp Val Ile 145 150 155 160
- Pro Val Gly Thr Thr Val His Leu Thr Pro Arg Pro Asp Glu Arg Thr 165 170 175
- Leu Leu Thr Glu Asn Ser Val Val Thr Ile Ala Ser Asn Tyr Gly Arg 180 185 190
- Tyr Leu Pro Ile Pro Ile Val Val Gln Gly Glu Lys Asn Thr Thr Ile 195 200 205
- Thr Thr Ser Pro Val Phe Ala Lys Asp Thr Asp Gln Gln His Arg Leu 210 215 220
- Tyr Ala Gly Arg Glu Arg Leu Gly Lys Thr Pro Phe Asp Val Ile Asp 225 230 235 240
- Leu Thr Gly Pro Gly Ile Glu Gly Val Ala Tyr Val Leu Pro Glu Ala 245 250 255
- Gln Ala Pro His Met Ser Arg Arg His Ser Ile Tyr Val Asn Arg Met 260 265 270
- Leu Val Ser Asp Gly Pro Ser Thr Val Leu Pro Asn Trp Ala Phe Phe 275 280 285
- Val Glu Cys Glu Ile Asn Ser Thr Asp Leu Glu Pro Thr Ala Ser Arg 290 295 300
- Glu Ala Leu Met Asp Asp Thr Ala Phe Ala Ala Thr Arg Glu His Ile 305 310 315 320
- Gly Glu Cys Ile Lys Ser Trp Leu Ile Asn Leu Ala Met Thr Lys Pro 325 330 335

- His Arg Val Arg Glu Phe Thr Ala Ile His Asp Leu Ala Leu Arg Glu 340 345 350
- Leu Cys Gln Ser Asp Ala Asp Leu Ala Glu Thr Met Leu Gly Leu Leu 355 360 365
- Thr Leu Glu Thr Ser Arg Gly Arg Ile Ser Ile Gly Glu Ile Thr Thr 370 375 380
- Leu Ser Ile Thr Glu Asp Val Ser Leu Gln Leu Ala Thr Thr Leu Asp 385 390 395 400
- Asp Phe Arg Gln Leu Asn Thr Ile Ala Arg Pro Asp Thr Leu Ile Ile 405 410 415
- Asn Gly Gly Tyr Ile His Asp Ser Asp Leu Ala Arg Leu Ile Pro Val 420 425 430
- His Tyr Pro Pro Leu Thr Val Ser Thr Ala Asp Leu Arg Glu Ser Met 435 440 445
- Asp Leu Met Glu Leu Pro Pro Leu Gln Asp Ile Glu Lys Ala Lys Ala 450 455 460
- Leu Asp Ala Gln Val Thr Glu Ser Leu Lys Asp Phe Gln Ile Lys Gly 465 470 475 480
- Ala Thr Arg Val Phe Glu Pro Ala Asp Val Pro Ala Val Val Ile Ile 485 490 495
- Asp Ser Lys Ala Gln Ala Ser Arg Asp Arg Asn Glu Thr Gln Ser Ala 500 505 510
- Thr Thr Asp Arg Trp Ala Asp Ile Leu Ala Thr Val Asp Asn Thr Leu 515 520 525
- Ser Arg Gln Thr Ala Asn Ile Pro Gln Asp Gln Gly Leu Ser Ala Leu 530 535 540
- Cys Leu Asn Trp Asn Asn Ser Leu Val Arg Lys Leu Ala Ser Thr Asp 545 550 555 560
- Asp Thr Ala Val Val Ser Arg Thr Val Arg Leu Leu Tyr Val Gln Ala 565 570 575
- Leu Leu Ser Ser Lys Arg Pro Leu Arg Val Lys Glu Arg Ala Leu Leu 580 585 590
- Asn Asp Ser Leu Ala Asp Leu Val Ser Leu Ser Leu Ser Ser Asp Ile 595 600 605 .

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cgt Arg	gat Asp	aat Asn	ttc Phe	caa Gln 10	Val	gac Asp	ctc Leu	ggc	ggc Gly 15	' Val	gtt Val	gat Asp	ctt Leu	ttg Leu 20	agt Ser	163
cgc Arg	cac His	att Ile	tat Tyr 25	tcc Ser	ggt Gly	ccg Pro	agg Arg	gtg Val 30	tat Tyr	gtg Val	cgt Arg	gag Glu	ttg Leu 35	ctg Leu	cag Gln	211
aat Asn	gcg Ala	gtt Val 40	gat Asp	gct Ala	tgt Cys	act Thr	gca Ala 45	cgt Arg	tct Ser	gaa Glu	cag Gln	ggt Gly 50	Glu	gag Glu	ggc Gly	259
tac Tyr	gag Glu 55	ccg Pro	agt Ser	att Ile	cgt Arg	att Ile 60	cgg Arg	ccg Pro	gtg Val	acc Thr	aag Lys 65	gat Asp	cgt Arg	gcc Ala	acg Thr	307
ttt Phe 70	tca Ser	ctg Leu	gtt Val	gat Asp	aat Asn 75	ggt Gly	acg Thr	ggc Gly	ctg Leu	acc Thr 80	gcg Ala	cag Gln	gag Glu	gcg Ala	cgg Arg 85	355
gaa Glu	ttg Leu	ctg Leu	gcg Ala	acg Thr 90	gtg Val	ggg Gly	cgg Arg	acg Thr	tcg Ser 95	aaa Lys	cgc Arg	gat Asp	gaa Glu	ttc Phe 100	ggt Gly	403
		cgg Arg														436
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/al	Asp	Leu	Leu 20	Ser	Arg	His	Ile	Tyr 25	Ser	Gly	Pro	Arg	Val	Tyr	Val	

Arg Glu Leu Leu Gln Asn Ala Val Asp Ala Cys Thr Ala Arg Ser Glu 35 40 45

Gln Gly Glu Glu Gly Tyr Glu Pro Ser Ile Arg Ile Arg Pro Val Thr 50 55 60

Lys Asp Arg Ala Thr Phe Ser Leu Val Asp Asn Gly Thr Gly Leu Thr 65 70 75 80

Ala Gln Glu Ala Arg Glu Leu Leu Ala Thr Val Gly Arg Thr Ser Lys 85 90 95

Arg Asp Glu Phe Gly Leu Gln Arg Glu Gly Arg Leu Gly Gln Phe Gly 100 105 110

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- tac ggc att ctc ggc gtc gat cgc aat gca acc gaa tca gag atc aaa 163 Tyr Gly Ile Leu Gly Val Asp Arg Asn Ala Thr Glu Ser Glu Ile Lys 10 15 20
- aag gca tac cga aag ctt gcc cgc aaa tac cac ccg gac gta aac cca 211 Lys Ala Tyr Arg Lys Leu Ala Arg Lys Tyr His Pro Asp Val Asn Pro 25 30 35
- ggt gag gaa gca gcg gag aaa ttc cgc gag gct tct gtt gcg cat gag 259 Gly Glu Glu Ala Ala Glu Lys Phe Arg Glu Ala Ser Val Ala His Glu 40 45
- gta ctc act gat ccg gat aag cgc cgc att gtt gat atg ggc ggt gac 307 Val Leu Thr Asp Pro Asp Lys Arg Arg Ile Val Asp Met Gly Gly Asp 55 60 65
- cca atg gag caa ggc ggc gga gct ggc ggt ggc ttc ggt gga ggc 355 Pro Met Glu Gln Gly Gly Gly Ala Gly Ala Gly Gly Phe Gly Gly Gly 75 80 85

ttc ggc ggc agc ggt gga ctg ggc gat atc ttc gat gcc ttc ttc ggc 403

63

Phe	Gly	Gly	Ser	Gly 90	_	Leu	Gly	Asp	Ile 95		Asp	Ala	Phe	Phe 100		
				Gly				cca Pro 110	Arg					Pro		451
			Leu					atc Ile								499
							Leu	gac Asp								547
								gac Asp			Pro					595
	_			_		-		cag Gln	-		_	-	_		_	643
		-	_			_		tgc Cys 190			-	-				691
				-		_		gag Glu	_	_	-	_		_		739
	_	_	-	-			_	aac Asn			_			_		787
								caa Gln	Gly							835
								gaa Glu								883
								ctg Leu 270								931
atg Met	ttc Phe	gat Asp 280	gca Ala	gcg Ala	ctt Leu	ggc Gly	acc Thr 285	gaa Glu	ttg Leu	gac Asp	gtg Val	gaa Glu 290	tcc Ser	ctc Leu	acc Thr	979
								cct Pro								1027
gtg Val	atc Ile	acc Thr	ttg Leu	gat Asp	ggt Gly	gaa Glu	ggc Gly	atg Met	ccg Pro	aag Lys	ctg Leu	cgc Arg	gca Ala	gaa Glu	ggc Gly	1075

310	315	320	325											
His Gly Asn Leu M		gat cta ttt gtg cca Asp Leu Phe Val Pro 335	, ,											
		gaa gaa atc cgc aac Glu Glu Ile Arg Asn 350												
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Ser Val Ala His Gl 50	lu Val Leu Thr 55	Asp Pro Asp Lys Arg 60	Arg Ile Val											
Asp Met Gly Gly As 65	sp Pro Met Glu 70	Gln Gly Gly Gly Ala 75	Gly Ala Gly 80											
	ly Phe Gly Gly B5	Ser Gly Gly Leu Gly 90	Asp Ile Phe 95											
Asp Ala Phe Phe Gl		Gly Gly Ser Arg Gly 105	Pro Arg Ser 110											
Arg Val Gln Pro Gl 115	y Ser Asp Thr 120	Leu Trp Arg Thr Ser 125	Ile Thr Leu											
Glu Glu Ala Tyr Ly 130	s Gly Ala Lys : 135	Lys Asp Leu Thr Leu 140	Asp Thr Ala											
Val Leu Cys Thr Ly 145	s Cys His Gly : 150	Ser Gly Ser Ala Ser 155	Asp Lys Lys 160											

Pro Val Thr Cys Gly Thr Cys Asn Gly Ala Gly Glu Ile Gln Glu Val 165 170 175

Gln Arg Ser Phe Leu Gly Asn Val Met Thr Ser Arg Pro Cys His Thr 180 185 190

Cys Asp Gly Thr Gly Glu Ile Ile Pro Asp Pro Cys Thr Glu Cys Ala 195 200 205

Ala Asp Gly Arg Val Arg Ala Arg Arg Asp Ile Val Ala Asn Ile Pro 210 215 220

Ala Gly Ile Gln Ser Gly Met Arg Ile Arg Met Ala Gly Gln Gly Glu 225 235 240

Val Gly Ala Gly Gly Pro Ala Gly Asp Leu Tyr Ile Glu Val Met 245 250 255

Val Arg Pro His Ala Ile Phe Thr Arg Asp Gly Asp Asp Leu His Ala 260 265 270

Ser Ile Lys Val Pro Met Phe Asp Ala Ala Leu Gly Thr Glu Leu Asp 275 280 285

Val Glu Ser Leu Thr Gly Glu Glu Val Lys Ile Thr Ile Pro Ala Gly 290 295 300

Thr Gln Pro Asn Asp Val Ile Thr Leu Asp Gly Glu Gly Met Pro Lys 305 310 315 320

Leu Arg Ala Glu Gly His Gly Asn Leu Met Ala His Val Asp Leu Phe 325 330 335

Val Pro Thr Asp Leu Asp Asp Arg Thr Arg Glu Leu Leu Glu Glu Ile 340 345 350

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Glu Ser Gly Phe Phe Asp Lys Leu Arg Asn Lys Phe Arg Lys 370 380

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Val Lys Ser Ser Val gag aag ctg agc gac acc cgt tca aag atc acc gtt gag gtt cca ttt 163 Glu Lys Leu Ser Asp Thr Arg Ser Lys Ile Thr Val Glu Val Pro Phe tct gaa ctg aag cca gag atc gac cag gca tac gcc gct cta gcg cag 211 Ser Glu Leu Lys Pro Glu Ile Asp Gln Ala Tyr Ala Ala Leu Ala Gln caa gtc cag atc cct ggt ttc cgt aag ggc aag gca ccg cgt cag ctt 259 Gln Val Gln Ile Pro Gly Phe Arg Lys Gly Lys Ala Pro Arg Gln Leu atc gac gca cgc ttc ggc cgt ggt gcg gtt ctg gag cag gtt gtc aac 307 Ile Asp Ala Arg Phe Gly Arg Gly Ala Val Leu Glu Gln Val Val Asn gac atg ctt cct aac cgc tac gca cag gca atc gaa gct gag ggc atc 355 Asp Met Leu Pro Asn Arg Tyr Ala Gln Ala Ile Glu Ala Glu Gly Ile 75 80 aag gca atc ggc cag cct aac gta gag gtc acc aag atc gaa gac aac 403 Lys Ala Ile Gly Gln Pro Asn Val Glu Val Thr Lys Ile Glu Asp Asn 95 gag ctc gtt gag ttc gtc gct gag gtt gac gtt cgc cca gag ttc gag 451 Glu Leu Val Glu Phe Val Ala Glu Val Asp Val Arg Pro Glu Phe Glu 105 110 ctt cct aag ttc gag gac atc act gtt gag gtc cca gct atc aag gct 499 Leu Pro Lys Phe Glu Asp Ile Thr Val Glu Val Pro Ala Ile Lys Ala gac gaa gag gca atc gaa gca gag ctc gag acc ctg cgt qca cgt ttc 547 Asp Glu Glu Ala Ile Glu Ala Glu Leu Glu Thr Leu Arg Ala Arg Phe 135 140 tcc acc ttg aag gat cac aac cac aag ctg aag aag ggt gag ttc gtc 595 Ser Thr Leu Lys Asp His Asn His Lys Leu Lys Lys Gly Glu Phe Val 155 160 acc atc aac atc acc gca agc att gac ggt gag aag att gaa gag gca 643 Thr Ile Asn Ile Thr Ala Ser Ile Asp Gly Glu Lys Ile Glu Glu Ala 170 acc act gag ggt ctg tcc tac gaa atc gga tct gac gat ctg att gac 691 Thr Thr Glu Gly Leu Ser Tyr Glu Ile Gly Ser Asp Asp Leu Ile Asp 190 ggc ctg gac aag gct ctg atc ggc gct aag aag gat gaa acc gta gag 739 Gly Leu Asp Lys Ala Leu Ile Gly Ala Lys Lys Asp Glu Thr Val Glu 205 ttc acc tct gag ctg gca aac ggc gag cac aag ggc aag gaa gct caa 787 Phe Thr Ser Glu Leu Ala Asn Gly Glu His Lys Gly Lys Glu Ala Gln

215 220 225

															ctg Leu	835
230			-		235			2 -		240		. 500			245	
					Glr					Phe			: atc			883
				Thr					Glu				aag Lys 275	Asn		931
			Ala					Val					ctt Leu			979
		Phe					Ser						gca Ala			1027
											Asp		gct Ala			1075
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													cag Gln			1219
													gac Asp			1267
cag Gln 390	Phe	Ile	Gly	Gln	ctg Leu 395	Gln	Gln	tcc Ser	Gly	Gln	Ile	gcg Ala	aac Asn	ctc Leu	ttc Phe 405	1315
													tgc Cys			1363
													gaa Glu 435			1411
ggt Gly	gaa Glu	gaa Glu 440	gaa Glu	gta Val	gct Ala	gag Glu	act Thr 445	gag Glu	tct Ser	gaa Glu	gct Ala	taaa	aact	tt		1457

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35 40 45

Ala Pro Arg Gln Leu Ile Asp Ala Arg Phe Gly Arg Gly Ala Val Leu 50 55 60

Glu Gln Val Val Asn Asp Met Leu Pro Asn Arg Tyr Ala Gln Ala Ile 65 70 75 . 80

Glu Ala Glu Gly Ile Lys Ala Ile Glý Gln Pro Asn Val Glu Val Thr 85 90 95

Lys Ile Glu Asp Asn Glu Leu Val Glu Phe Val Ala Glu Val Asp Val 100 105 110

Arg Pro Glu Phe Glu Leu Pro Lys Phe Glu Asp Ile Thr Val Glu Val 115 120 125

Pro Ala Ile Lys Ala Asp Glu Glu Ala Ile Glu Ala Glu Leu Glu Thr 130 135 140

Leu Arg Ala Arg Phe Ser Thr Leu Lys Asp His Asn His Lys Leu Lys 145 150 155 160

Lys Gly Glu Phe Val Thr Ile Asn Ile Thr Ala Ser Ile Asp Gly Glu 165 170 175

Lys Ile Glu Glu Ala Thr Thr Glu Gly Leu Ser Tyr Glu Ile Gly Ser 180 185 190

Asp Asp Leu Ile Asp Gly Leu Asp Lys Ala Leu Ile Gly Ala Lys Lys 195 200 205

Asp Glu Thr Val Glu Phe Thr Ser Glu Leu Ala Asn Gly Glu His Lys 210 215 220

Gly Lys Glu Ala Gln Ile Ser Val Glu Ile Thr Ala Thr Lys Gln Arg 225 230 235 240

Glu Leu Pro Glu Leu Asp Asp Glu Phe Ala Gln Leu Ala Ser Glu Phe 245 250 255

Asp Thr Ile Glu Glu Leu Arg Glu Ser Thr Val Ser Asp Val Glu Ala Lys Gln Lys Asn Glu Gln Ala Ala Ile Arg Asp Glu Val Leu Ala 280 Ala Ala Leu Gly Glu Ala Asp Phe Ala Leu Pro Gln Ser Ile Val Asp 295 Glu Gln Ala His Ser Gln Leu His Gln Leu Leu Gly Glu Leu Ala His Asp Asp Ala Ala Leu Asn Ser Leu Leu Glu Ala Gln Gly Thr Thr Arg 330 Glu Glu Phe Asp Lys Lys Asn Val Glu Asp Ala Glu Lys Ala Val Arg Thr Gln Leu Phe Leu Asp Thr Leu Ser Glu Val Glu Glu Pro Glu Val 360 Ser Gln Gln Glu Leu Thr Asp His Ile Leu Phe Thr Ala Gln Ser Tyr 375 Gly Met Asp Pro Asn Gln Phe Ile Gly Gln Leu Gln Gln Ser Gly Gln 390 395 Ile Ala Asn Leu Phe Ser Asp Val Arg Arg Gly Lys Ala Leu Ala Gln Ala Ile Cys Arg Val Asn Val Lys Asp Ser Glu Gly Asn Glu Ile Asp Pro Lys Glu Tyr Phe Gly Glu Glu Glu Val Ala Glu Thr Glu Ser Glu Ala <210> 43 <211> 826 <212> DNA <213> Corynebacterium glutamicum <220> <221> CDS <222> (101)..(826) <223> RXN03038 gcgcggaaaa caccaagtaa gccttacagt ccgacagcct catagcggat gggataagtt 60

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gag Glu	tta Leu	aca Thr	gtç Val	g cgt Arg 10	Lys	a gga s Gly	att / Ile	tco Ser	c cgc Arc	y Val	c cto Lev	tcg Ser	g gta Val	a gcg . Ala 20	g gtt a Val)	163
gct Ala	agt Ser	tca Ser	ato Ile 25	: Gly	tto Phe	gga Gly	act Thr	gta Val	Let	g aca Thr	ggc Gly	acc Thr	ggc Gl ₃ 35	/ Ile	gca Ala	211
gca Ala	gct Ala	caa Gln 40	Asp	tct Ser	gca Ala	ttt Phe	gac Asp 45	Tyr	ggt Gly	atg Met	gat Asp	cca Pro 50	Asn	atg Met	aac Asn	259
		Pro				atc Ile 60	Lys									307
ctt Leu 70	ccc Pro	tac Tyr	ttc Phe	gga Gly	agt Ser 75	aaa Lys	ttg Leu	acc Thr	agc Ser	tgg Trp 80	Gly	tca Ser	tca Ser	tat Tyr	gcc Ala 85	355
Thr	Ala	Ser	Ser	Gly 90	Val	gtg Val	Thr	Ser	Ala 95	Leu	Pro	Gln	Tyr	Thr 100	Asp	403
Pro	Arg	Tyr	Pro 105	Leu	Gly	aaa Lys	Asp	Asp 110	Leu	Pro	Lys	Ala	Thr 115	Ile	Asp	.451
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Thr 150	Ile	Pro	Leu	Val	Trp 155	gtt Val	Val	Pro	Glu	Asp 160	Asn	Thr	Val	Pro	Gly 165	595
Pro	Thr	Val	Tyr	Ala 170	Leu	gga Gly	Gly	Gly	Asp 175	Gly	Gly	Gln	Gly	Gly 180	Gln	643
Asn	Trp	Val	Thr 185	Arg	Thr	gac Asp	Leu	Glu 190	Glu	Leu	Thr	Ser	Asp 195	Asn	Asn	691
Ile	Asn	Leu 200	Ile	Met	Pro		Leu 205	Gly	Ser	Phe	Ser	Phe 210	Tyr	Ser	Asp	739
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826

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<211> 242

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<213> Corynebacterium glutamicum

<400> 44

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Leu Ser Val Ala Val Ala Ser Ser Ile Gly Phe Gly Thr Val Leu Thr 20 25 30

Gly Thr Gly Ile Ala Ala Ala Gln Asp Ser Ala Phe Asp Tyr Gly Met 35 40 45

Asp Pro Asn Met Asn Tyr Asn Pro Ile Asp Asp Ile Lys Asp Arg Pro 50 60

Glu Gly Leu Ser Asn Leu Pro Tyr Phe Gly Ser Lys Leu Thr Ser Trp 65 70 75 80

Gly Ser Ser Tyr Ala Thr Ala Ser Ser Gly Val Val Thr Ser Ala Leu 85 90 95

Pro Gln Tyr Thr Asp Pro Arg Tyr Pro Leu Gly Lys Asp Asp Leu Pro 100 105 110

Lys Ala Thr Ile Asp Met Glu Pro Glu Val Leu Ala Arg Leu Glu Arg 115 120 . 125

Phe Val Gly Val Asp Gly Asp Arg Ile Arg Gln Ile Asn Ala Tyr Ser 130 135 140

Pro Ser Met Gly Arg Thr Ile Pro Leu Val Trp Val Val Pro Glu Asp 145 150 155 160

Asn Thr Val Pro Gly Pro Thr Val Tyr Ala Leu Gly Gly Gly Asp Gly 165 170 175

Gly Gln Gly Gln Asn Trp Val Thr Arg Thr Asp Leu Glu Glu Leu 180 185 190

Thr Ser Asp Asn Asn Ile Asn Leu Ile Met Pro Met Leu Gly Ser Phe 195 200 205

Ser Phe Tyr Ser Asp Trp Ala Arg Glu Ser Gln Ser Met Gly Cys Ala 210 215 220

Gln Gln Trp Glu Thr Leu Leu Met His Glu Leu Pro Glu Pro Leu Val 225 230 235 240

Ala Ala

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			Val					Asp			cgc Arg					144
											gtc Val 60					192
_	-							_	_		gca Ala					240
											cgc Arg					288
	_		_	_							atg Met		_			336
		_			-	_		_		_	agc Ser	-		-		384
											gaa Glu 140					432
											agc Ser					480
											acg Thr					528

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ctc	taca	tct	tcgc	cggt	tc c	ggtg	tgtt	c tc	tgaa	ctag				ggt Gly		115
										aac Asn						163
	-		-	_	_				_	acc Thr				_	-	211
										aac Asn						259
				-		-				gaa Glu				-		307
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gtc Val		tgat	gtga	igc c	ttgg	cacc	n gt	:g								432

<210> 48 <211> 103 <212> PRT <213> Corynebacterium glutamicum

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Pro 70	Lys	Ser	Asn	Glu	75		Asn	Pro	Asp	61 o 80		. Gly	Lys	Arg	Ser 85	
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gca Ala	gtg Val	acc Thr	ttg Leu 105	gac Asp	ggt Gly	ttg Leu	cga Arg	cag Gln 110	tgg Trp	ggg Gly	acc Thr	ttg Leu	aac Asn 115	Trp	gaa Glu	451
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ccc Pro	ctt Leu 135	act Thr	cag Gln	cga Arg	cag Gln	act Thr 140	Phe	caa Gln	ggt Gly	ggt Gly	gac Asp 145	aac Asn	tac Tyr	tac Tyr	aac Asn	547
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gaa Glu	ctt Leu	ggc Gly	ggc Gly	tcg Ser 170	aat Asn	cat His	gcc Ala	att Ile	ggc Gly 175	atc Ile	ccg Pro	atc Ile	act Thr	aat Asn 180	gag Glu	643
cta Leu	cct Pro	agc Ser	ggt Gly 185	act Thr	gag Glu	tat Tyr	ttt Phe	tac Tyr 190	aat Asn	aat Asn	ttc Phe	tcc Ser	aat Asn 195	gga Gly	aca Thr	691
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Gln .	cgg Arg 215	gtg Val	tgg Trp	gat Asp	gcg Ala	ttg Leu 220	.ggt Gly	cgg Arg	gag Glu	acg Thr	ggt Gly 225	cgt Arg	tta Leu	ggt Gly	ttt Phe	787
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Val Cys Gly Arg Ile Leu Asp Thr Tyr Arg Gln Val Gly Gly Gln Leu 50 60

Ser Trp Leu Gly Pro Pro Lys Ser Asn Glu Leu Thr Asn Pro Asp Gly 65 70 75 80

Val Gly Lys Arg Ser Glu Phe Phe Gly Gly Ala Ile Tyr Trp His Pro 85 90 95

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Asp Asn Tyr Tyr Asn Pro Leu Thr Gly Gly Ala Val Trp Gly Asp Ile 145 150 155 160

Lys Gln Arg Tyr Glu Glu Leu Gly Gly Ser Asn His Ala Ile Gly Ile 165 170 175

Pro Ile Thr Asn Glu Leu Pro Ser Gly Thr Glu Tyr Phe Tyr Asn Asn 180 185 190

Phe Ser Asn Gly Thr Ile Ser Trp Arg Asn Asp Arg Gln Thr Arg Phe 195 200 205

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<222> (101)..(1681)

<223> RXN03054

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	wo	01/0	0804	į													PC	T/IB00/00
													1					5
aa Ly	ng go /s A]	et g La A	jca Ma	ggc Gly	gt Va	1 11	t go e Al	t go a Al	a go .a Al	a Le	t c u L	tt q eu V	gtt /al	gca Ala	gg Gl	y Gl	t at y Il	a 163 e
gc Al	a co a Pr	t g	tg al	gca Ala 25	Gli	g gg n Gl	g ca y Gl	a go n Al	a Se	r Gl	ig gi .n Va	tg g al V	gtc /al	aca Thr	cc Pr	o Gl	a ga u As _j	c 211 p
ca Gl	a ga n As	p A	cg la 40	tat Tyr	gtt Val	ca: Gl:	a ca n Gl	g tt n Ph 4	e Hi	c ca s Hi	c ga s G]	aa g lu G	igg :ly	aat Asn 50	Th	c cc r Pr	a cci o Pro	t 259
gt Va	g gt 1 Va 5	I A	ac (ggg Gly	gtç Val	ggt Gly	gge Gly 60	у Ту	c ac r Th	t ga r Gl	g ca u Gl	n G	aa lu 65	atc Ile	gcc Ala	c gad a Glo	g ato u Ile	307
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cto Le	ati a Ile	t co e Pr	eg g	ggt Gly	gag Glu 90	Met	tgg Trp	tca Ser	a gat Asp	Lys	s Va	g ga 1 G	ag lu	ctg Leu	cca Pro	gta Val	a act L Thr	403
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_	_				aat Asn					Gly						1603
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Val	Thr	Pro 35	Glu	Asp	Gln	Asp	Ala 40	Tyr	Val	Gln	Gln	Phe 45	His	His	Glu	
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Glu	Leu	Pro	Val 100	Thr	Ile	Asp	Lys	Ala 105	Ala	Ala	Asp	Glu	Ala 110	Glu	Ile	
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Arg Gln Arg Phe Met Asn Gly Phe Val Tyr Trp His Pro Thr Thr Gly 180 185 190

Ala His Ala Val Asn Asn Tyr Ser Ala Gln Val Trp Glu Arg Asn Gly 195 200 205

Trp Glu Ser Gly Trp Met Gly Tyr Pro Thr Gly Gly Glu Val Pro Val * 210 215 220

Asn Gly Ser Asn Pro Ile Asp Gly Glu Leu Ser Gly Trp Val Gln Thr 225 230 235 240

Phe Gln Gly Gly Arg Val Tyr Arg Ser Pro Val Leu Asp Gly Phe Gln 245 250 255

Val Ala Ser Ile Asn Gly Leu Ile Leu Asp Lys Trp Leu Glu Leu Gly 260 265 270

Gly Pro Asp Ser Asp Leu Gly Phe Pro Ile Ala Asp Glu Ala Val Thr 275 280 285

Ala Asp Gly Val Gly Arg Phe Ser Val Phe Gln Asn Gly Val Val Tyr 290 295 300

Trp His Pro Gln His Gly Ala His Pro Ile Leu Gly Asn Ile Tyr Ser 305 310 315 320

Ile Trp Arg Glu Glu Gly Ala Glu Ser Gly Glu Phe Gly Tyr Pro Ile 325 330 335

Gly Asp Pro Glu Lys Tyr Thr Glu Asn Met Ala Asn Gln Val Phe Glu 340 345 350

Lys Gly Glu Leu Ala Ala Asn Leu Tyr Pro Asn Pro Leu Glu Ala Phe 355 360 365

Ile Glu Phe Leu Pro Phe Ala Asn Leu Glu Glu Ala Ile Glu Tyr Phe 370 375 380

Glu Asn Gly Leu Ser Asn Ser Arg Val Glu Ala Asn Ser Leu Asn Ala 385 390 395 400

Lys Lys Asp Ser Ile Gln Cys Gln Ser Gln Ser Ala Asn Ile His Val $405 \hspace{1.5cm} 410 \hspace{1.5cm} 415$

Arg Thr Lys Ser Asp Gly Val Gly Ile Arg Val Pro Lys Ile Gly Phe 420 425 430

Lys Ala Arg Met Asp Cys Asp Leu Pro Gly Thr Val Ser Asp Val Val 435 440 445

Gly Tyr Gly Trp Ile Tyr Tyr Asp Tyr Trp Gly Arg Trp Ala Gln Ala

450 455 460

Ala Tyr Ala Gln Gln Phe Phe Gly Asn Arg Asn Ser Val Val Gln Thr 465 470 475 480

Asn Leu Glu Ala Gly Cys Ser Gly Glu Lys Asn Thr Leu Phe Trp Gly 485 490 495

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<213> Corynebacterium glutamicum

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tcg ggt gct tcc act acc tct acc tct tct tat gag gct aag cag gta 211 Ser Gly Ala Ser Thr Thr Ser Thr Ser Ser Tyr Glu Ala Lys Gln Val 25 30 35

tct aca cag aag aag tca tcc ggt tcg gat tct aag cct ggc ggc ggt 259 Ser Thr Gln Lys Lys Ser Ser Gly Ser Asp Ser Lys Pro Gly Gly Gly 40 45

gtt att tct ttt ctg cct gag gtt gtg gga gaa gtc cgt aag gtt att 307 Val Ile Ser Phe Leu Pro Glu Val Val Gly Glu Val Arg Lys Val Ile

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Trp Pro Thr Ala Arg Gln Met Val Thr Tyr Thr Leu Val Val Leu Gly
70 80 85

ttc ttg att gtt ttg acc gct ttg gtg tct ggt gtg gat ttc cta gct 403
Phe Leu Ile Val Leu Thr Ala Leu Val Ser Gly Val Asp Phe Leu Ala
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ttt 456

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<213> Corynebacterium glutamicum

<400> 54

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Glu Ala Lys Gln Val Ser Thr Gln Lys Lys Ser Ser Gly Ser Asp Ser 35 40 45

Lys Pro Gly Gly Val: Ile Ser Phe Leu Pro Glu Val Val Gly Glu
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Val Arg Lys Val Ile Trp Pro Thr Ala Arg Gln Met Val Thr Tyr Thr 65 70 75 80

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Val Asp Phe Leu Ala Gly Leu Gly Val Glu Lys Ile Leu Thr Pro 100 105 110

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<223> RXN02462

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Met Thr Lys Asp Val

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25 30 35

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					Phe					ctt Leu					355
				His						aaa Lys					403
			Asn							acc Thr					451
_						_		-		ggt Gly		_			499
										gac Asp 145					547
		_			_	-	-	-	_	acc Thr	-	_			595
			_	-		-	-	_	-	gac Asp	_		-	-	643
										acc Thr					691
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										gca Ala 225					787
			Pro							acc Thr					835
		Asp					Gly			gaa Glu					883

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			Ala					Let					Gln		tgc Cys	979
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												acc Thr				1171
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				Leu								aaa Lys				1555

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85 90 95

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- Gly Thr Ala Glu Thr Glu Ala Ala Glu Leu Asn Gln Ile Tyr Lys Leu 130 135 140
- Asp Val Ile Ala Ile Pro Thr Asn Arg Pro Asn Gln Arg Glu Asp Leu 145 150 155 160
- Thr Asp Leu Val Tyr Lys Thr Gln Glu Ala Lys Phe Ala Ala Val Val 165 170 175
- Asp Asp Ile Ala Glu Arg Thr Glu Lys Gly Gln Pro Val Leu Val Gly 180 185 190
- Thr Val Ser Val Glu Arg Ser Glu Tyr Leu Ser Gln Leu Leu Thr Lys 195 200 205
- Arg Gly Ile Lys His Asn Val Leu Asn Ala Lys His His Glu Gln Glu 210 215 220
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- Thr Asn Met Ala Gly Arg Gly Thr Asp Ile Val Leu Gly Gly Asn Pro 245 250 255
- Glu Ile Leu Leu Asp Ile Lys Leu Arg Glu Arg Gly Leu Asp Pro Phe 260 265 270
- Glu Asp Glu Glu Ser Tyr Gln Glu Ala Trp Asp Ala Glu Leu Pro Ala 275 280 285
- Met Lys Gln Arg Cys Glu Glu Arg Gly Asp Lys Val Arg Glu Ala Gly 290 295 300
- Gly Leu Tyr Val Leu Gly Thr Glu Arg His Glu Ser Arg Arg Ile Asp 305 310 315 320
- Asn Gln Leu Arg Gly Arg Ser Ala Arg Gln Gly Asp Pro Gly Ser Thr 325 330 335
- Arg Phe Tyr Leu Ser Met Arg Asp Asp Leu Met Val Arg Phe Val Gly 340 345 350
- Pro Thr Met Glu Asn Met Met Asn Arg Leu Asn Val Pro Asp Asp Val 355 360 365
- Pro Ile Glu Ser Lys Thr Val Thr Asn Ser Ile Lys Gly Ala Gln Ala 370 380
- Gln Val Glu Asn Gln Asn Phe Glu Met Arg Lys Asn Val Leu Lys Tyr

385 390 395 400

Asp Glu Val Met Asn Glu Gln Arg Lys Val Ile Tyr Ser Glu Arg Arg 405 410 415

Glu Ile Leu Glu Ser Ala Asp Ile Ser Arg Tyr Ile Gln Asn Met Ile 420 425 430

Glu Glu Thr Val Ser Ala Tyr Val Asp Gly Ala Thr Ala Asn Gly Tyr 435 440 445

Val Glu Asp Trp Asp Leu Asp Lys Leu Trp Asn Ala Leu Glu Ala Leu 450 455 460

Tyr Asp Pro Ser Ile Asn Trp Thr Asp Leu Val Glu Gly Ser Glu Tyr 465 470 475 480

Gly Lys Pro Gly Glu Leu Ser Ala Glu Asp Leu Arg Thr Ala Leu Val 485 490 495

Asn Asp Ala His Ala Glu Tyr Ala Lys Leu Glu Glu Ala Val Ser Ala 500 505 510

Ile Gly Gly Glu Ala Gln Ile Arg Asn Ile Glu Arg Met Val Leu Met 515 520 525

Pro Val Ile Asp Thr Lys Trp Arg Glu His Leu Tyr Glu Met Asp Tyr 530 535 540

Leu Lys Glu Gly Ile Gly Leu Arg Ala Met Ala Gln Arg Asp Pro Leu 545 550 560

Val Glu Tyr Gln Lys Glu Gly Gly Asp Met Phe Asn Gly Met Lys Asp 565 570 575

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1 5

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				ttg Leu												787

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				Thr					Thr			ttc Phe				931
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			_			-	_				_	cgc Arg			-	1171
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												aag Lys				1267
							Ala	Leu	Val		Ile	ttc Phe				1315
												ctg Leu				1363
ggc Gly	gtg Val	ttg Leu	gtc Val 425	tac Tyr	ggc Gly	ctt Leu	Leu	gta Val 430	ctg Leu	ctg Leu	gga Gly	cgc Arg	tgg Trp 435	atc Ile	gga Gly	1411
						Gly						atc Ile 450				1459

		Ala			ttc Phe		Val					Ile				1507
					tcc Ser 475											1555
agc Ser	gcc Ala	aag Lys	cgc Arg	acc Thr 490	atc Ile	gtc Val	aca Thr	ggc Gly	aac Asn 495	atg Met	gtc Val	act Thr	ttg Leu	ctc Leu 500	ggc Gly	1603
gct Ala	atc Ile	gtg Val	att Ile 505	tac Tyr	ttg Leu	ctc Leu	gcg Ala	gtc Val 510	ggc Gly	gaa Glu	gtc Val	aag Lys	ggc Gly 515	ttt Phe	gcc Ala	1651
		_		-	acc Thr		-		-		_	_				1699
atc Ile	acg Thr 535	gca Ala	cca Pro	ctg Leu	gtt Val	atc Ile 540	ctg Leu	gca Ala	tca Ser	cgc Arg	aac Asn 545	cca Pro	ttc Phe	ttt Phe	gcc Ala	1747
aag Lys 550	tca Ser	tcg Ser	gtc Val	aac Asn	ggc Gly 555	atg Met	gga Gly	cga Arg	gtg Val	atg Met 560	aag Lys	ctc Leu	gtt Val	gaa Glu	gaa Glu 565	1795
			Asn		gaa Glu											1843 .
					gca Ala											1891
act Thr	gac Asp	aat Asn 600	tct Ser	gaa Glu	gca Ala	Pro	ggc Gly 605	acc Thr	gat Asp	acg Thr	aac Asn	caa Gln 610	gag Glu	gag Glu	gag Glu	1939
aag Lys	tago	catg	ac t	gatt	ccca	g ac	t									1965

. <210> 58

<211> 614

<212> PRT

<213> Corynebacterium glutamicum

<400> 58

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Arg Ser Ala Thr Pro Lys Leu Gly Ile Asp Leu Gln Gly Gly Thr Arg

Val Thr Leu Val Pro Gln Gly Gln Asp Pro Thr Gln Asp Gln Leu Asn 35 40 45

- Gln Ala Arg Thr Ile Leu Glu Asn Arg Val Asn Gly Met Gly Val Ser 50 55 60
- Gly Ala Ser Val Val Ala Asp Gly Asn Thr Leu Val Ile Thr Val Pro 65 70 75 80
- Gly Glu Asn Thr Ala Gln Ala Gln Ser Leu Gly Gln Thr Ser Gln Leu 85 90 95
- Leu Phe Arg Pro Val Gly Gln Ala Gly Met Pro Asp Met Thr Thr Leu 100 . 105 110
- Met Pro Glu Leu Glu Glu Met Ala Asn Arg Trp Val Glu Tyr Gly Val 115 120 125
- Ile Thr Glu Glu Gln Ala Asn Ala Ser Leu Glu Glu Met Asn Thr Ala
 130 135 140
- Val Ala Ser Thr Thr Ala Val Glu Glu Glu Glu Ala Thr Glu Pro Glu 145 150 155 160
- Pro Val Thr Val Ser Ala Thr Pro Met Asp Glu Pro Ala Asn Ser Ile 165 170 175
- Glu Ala Thr Gln Arg Arg Gln Glu Ile Thr Asp Met Leu Arg Thr Asp 180 185 190
- Arg Gln Ser Thr Asp Pro Thr Val Gln Ile Ala Ala Ser Ser Leu Met 195 200 205
- Gln Cys Thr Thr Asp Glu Met Asp Pro Leu Ala Gly Thr Asp Asp Pro 210 215 220
- Arg Leu Pro Leu Val Ala Cys Asp Pro Ala Val Gly Gly Val Tyr Val 225 230 235 240
- Leu Asp Pro Ala Pro Leu Leu Asn Gly Glu Thr Asp Glu Glu Asn Gly 245 250 255
- Ala Arg Leu Thr Gly Asn Glu Ile Asp Thr Asn Arg Pro Ile Thr Gly
 260 265 270
- Gly Phe Asn Ala Gln Ser Gly Gln Met Glu Ile Ser Phe Ala Phe Lys 275 280 285
- Ser Gly Asp Gly Glu Glu Gly Ser Ala Thr Trp Ser Ser Leu Thr Ser 290 295 300
- Gln Tyr Leu Gln Gln Gln Ile Ala Ile Thr Leu Asp Ser Gln Val Ile 305 310 315 320
- Ser Ala Pro Val Ile Gln Ser Ala Thr Pro Val Gly Ser Ala Thr Ser 325 330 335

Ile Thr Gly Asp Phe Thr Gln Thr Glu Ala Gln Asp Leu Ala Asn Asn 340 345 350

Leu Arg Tyr Gly Ala Leu Pro Leu Ser Phe Ala Gly Glu Asn Gly Glu 355 360 365

Arg Gly Gly Thr Thr Thr Val Pro Pro Ser Leu Gly Ala Ala Ser 370 375 380

Leu Lys Ala Gly Leu Ile Ala Gly Ile Val Gly Ile Ala Leu Val Ala 385 390 395 400

Ile Phe Val Phe Ala Tyr Tyr Arg Val Phe Gly Phe Val Ser Leu Phe 405 410 415

Thr Leu Phe Ala Ala Gly Val Leu Val Tyr Gly Leu Leu Val Leu Leu 420 425 430

Gly Arg Trp Ile Gly Tyr Ser Leu Asp Leu Ala Gly Ile Ala Gly Leu 435 440 445

Ile Ile Gly Ile Gly Thr Thr Ala Asp Ser Phe Val Val Phe Tyr Glu 450 455 460

Arg Ile Lys Asp Glu Ile Arg Glu Gly Arg Ser Phe Arg Ser Ala Val 465 470 475 480

Pro Arg Ala Trp Glu Ser Ala Lys Arg Thr Ile Val Thr Gly Asn Met 485 490 495

Val Thr Leu Gly Ala Ile Val Ile Tyr Leu Leu Ala Val Gly Glu 500 505 510

Val Lys Gly Phe Ala Phe Thr Leu Gly Leu Thr Thr Val Phe Asp Leu 515 520 525

Val Val Thr Phe Leu Ile Thr Ala Pro Leu Val Ile Leu Ala Ser Arg 530 535 540

Asn Pro Phe Phe Ala Lys Ser Ser Val Asn Gly Met Gly Arg Val Met 545 550 · 555 560

Lys Leu Val Glu Glu Arg Arg Ala Asn Gly Glu Leu Asp Glu Pro Glu 565 570 575

Tyr Leu Lys Lys Ile His Ala Lys Asn Ala Ala Ala Asp Lys Ala Ser 580 585 590

Thr Asp Asn Ser Ser Thr Asp Asn Ser Glu Ala Pro Gly Thr Asp Thr 595 600 605

Asn Gln Glu Glu Glu Lys 610

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170 175 180

tta gtt ccc gat gcg ttc ctc att ggc gaa ggt cgc ttc tcc aac cct
Leu Val Pro Asp Ala Phe Leu Ile Gly Glu Gly Arg Phe Ser Asn Pro
185 190 195

gcg gat gtg gcg cac ggt cgt ctc att ggt gcc aac gcg atc atc gtg 739 Ala Asp Val Ala His Gly Arg Leu Ile Gly Ala Asn Ala Ile Ile Val 200 205 2·10

ggc acc gca atc act gac cct ggt ttc atc act gga cag ttc gcg tca 787 Gly Thr Ala Ile Thr Asp Pro Gly Phe Ile Thr Gly Gln Phe Ala Ser 215 220 225

ctg ttg cac tagcacttag tccagcgctg cac 819 Leu Leu His 230

<210> 60

<211> 232

<212> PRT

<213> Corynebacterium glutamicum

<400> 60

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1 5 10 15

Gln Leu Ile Val Ser Val Gln Ala Pro Asp Gly His Ala Met Arg Asp 20 25 30

Thr His Thr Leu Thr His Val Ala Ala Cys Val Asp Gly Gly Ala 35 40 45

Pro Ala Ile Arg Cys Gly Gly Tyr Gly Gly Leu Glu Asp Ile Arg Ser 50 60

Ile Ser Asn Arg Val Asp Val Pro Val Phe Gly Leu Thr Lys Glu Gly 65 70 75 80

Ser Glu Gly Val Tyr Ile Thr Pro Thr Arg Asp Ser Val Arg Ala Val 85 90 95

Ala Glu Ser Gly Ala Thr Val Val Cys Ala Asp Ala Thr Phe Arg Pro 100 105 110

Arg Pro Asp Gly Ser Thr Phe Ala Glu Leu Val Thr Val Ala His Asp 115 120 125

Ser Gly Ile Leu Ile Met Ala Asp Cys Ala Thr Pro Glu Glu Val Leu 130 135 140

Ser Ala His Lys Ala Gly Ala Asp Phe Val Ser Thr Thr Leu Ala Gly 145 150 155 160

Tyr Thr Glu His Arg Glu Lys Thr Val Gly Pro Asp Phe Asp Cys Leu 165 170 175

Arg Glu Ala Arg Glu Leu Val Pro Asp Ala Phe Leu Ile Gly Glu Gly Arg Phe Ser Asn Pro Ala Asp Val Ala His Gly Arg Leu Ile Gly Ala 200 Asn Ala Ile Ile Val Gly Thr Ala Ile Thr Asp Pro Gly Phe Ile Thr 215 Gly Gln Phe Ala Ser Leu Leu His 230 <210> 61 <211> 1219 <212> DNA <213> Corynebacterium glutamicum <220> <221> CDS <222> (48)..(1196) <223> RXN01863 <400> 61 ggtatcatac cgatatgaac caaatagaaa gaaggaagtt taagacgatg aat agc Met Asn Ser gtc aaa ttg aag caa cct gtt agc att tac aat gat cca tgg gaa tca 104 Val Lys Leu Lys Gln Pro Val Ser Ile Tyr Asn Asp Pro Trp Glu Ser tat aac gat gtt aaa gaa cat ggc caa tta act tta agt aac atc gaa 152 Tyr Asn Asp Val Lys Glu His Gly Gln Leu Thr Leu Ser Asn Ile Glu 30 ttt aca act aca aat ctt tgt aat atg cgt tgt agc cac tgt gca gtt 200 Phe Thr Thr Asn Leu Cys Asn Met Arg Cys Ser His Cys Ala Val ggt tat act tta caa act gtc gac ccc gag cct tta gat atg gac tta Gly Tyr Thr Leu Gln Thr Val Asp Pro Glu Pro Leu Asp Met Asp Leu 60 att tat cgt aga ctt gat gaa att cca aat ctg cga acg atg tca att 296 Ile Tyr Arg Arg Leu Asp Glu Ile Pro Asn Leu Arg Thr Met Ser Ile 75 aca ggt ggc gaa cca atg ttt tct aaa aag tct att aga aat gtt gtt 344 Thr Gly Gly Glu Pro Met Phe Ser Lys Lys Ser Ile Arg Asn Val Val aaa cct cta tta aag tat gca cat cat cga ggt ata tat aca caa atg 392 Lys Pro Leu Leu Lys Tyr Ala His His Arg Gly Ile Tyr Thr Gln Met 105

					Let					Tyr			att Ile			440
				Met					Asn				act Thr 145	Asp		488
			Val					Met					ccg Pro			536
		Leu											cgt Arg			584 .
						Val							aat Asn			632
_					_					-	_	_	cat His	-	_	680
	_	_	-						_			_	gac Asp 225		_	728
													aca Thr			776
													ttt Phe			824
													aag Lys			872
													gac Asp			920
													gta Val 305			968
	-			-	-					-			caa Gln		-	1016
			-	-		_				Ser		-	ctt Leu	-		1064
tca	tta	aat	tgt	cat	tgt	tcc	gag	ttt	agt	tgt	tta	gga	cca	aat	gtt	1112

Ser Leu Asn Cys His Cys Ser Glu Phe Ser Cys Leu Gly Pro Asn Val 340 345 350 355

ctt gtt aaa aat atg tac tat ccg aat atg gat ttt aaa gat aat gag 1160 Leu Val Lys Asn Met Tyr Tyr Pro Asn Met Asp Phe Lys Asp Asn Glu 360 365 370

cgt cat atg cac aaa caa cca caa att ata caa ttt taaaaactct 1206 Arg His Met His Lys Gln Pro Gln Ile Ile Gln Phe 375 380

taattatgcg gag 1219

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<211> 383

<212> PRT

<213> Corynebacterium glutamicum

<400> 62

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Trp Glu Ser Tyr Asn Asp Val Lys Glu His Gly Gln Leu Thr Leu Ser
20 25 30

Asn Ile Glu Phe Thr Thr Asn Leu Cys Asn Met Arg Cys Ser His 35 40 45

Cys Ala Val Gly Tyr Thr Leu Gln Thr Val Asp Pro Glu Pro Leu Asp 50 55 60

Met Asp Leu Ile Tyr Arg Arg Leu Asp Glu Ile Pro Asn Leu Arg Thr 65 70 75 80

Met Ser Ile Thr Gly Gly Glu Pro Met Phe Ser Lys Lys Ser Ile Arg 85 90 95

Asn Val Val Lys Pro Leu Leu Lys Tyr Ala His His Arg Gly Ile Tyr 100 105 110

Thr Gln Met Asn Ser Asn Leu Thr Leu Pro Gln Asp Arg Tyr Leu Asp 115 120 125

Ile Ala Glu Tyr Ile Asp Val Met His Ile Ser His Asn Trp Gly Thr 130 140

Thr Asp Glu Phe Ala Asn Val Gly Phe Gly Ala Met Lys Lys Gln Pro 145 150 155 160

Pro Leu Lys Ala Lys Leu Lys Leu Tyr Glu Gln Met Ile Ser Asn Ala 165 170 175

Arg Thr Leu Ser Glu Gln Gly Met Phe Val Ser Ala Glu Thr Met Leu 180 . 185 190

Asn Gln Ser Thr Leu Pro His Leu Arg Lys Ile His Gln Glu Val Val

99

W O 01/00004													rcı			
		195					200					205				
His	Asp 210	Met	Lys	Cys	Ser	Arg 215	His	Glu	Ile	His	Pro 220	Met	Tyr	Pro	Ala	
Asp 225	Phe	Ala	Ser	Gln	Leu 230	Asn	Val	Leu	Thr	Leu 235	Ala	Glu	Met	Lys	Lys 240	
Thr	Ile	His	Asp	Ile 245	Leu	Asp	Phe	Arg	Asp 250	Glu	Asp	Ile	Trp	Met 255	Leu	
Phe	Gly	Thr	Leu 260	Pro	Val	Phe	Pro	Cys 265	Leu	Lys	Asp	Asp	Glu 270	Asp	Gln	
Lys	Leu	Leu 275	Ser	Arg	Leu	Arg	Asn 280		Asn	Asn	Val	Thr 285	Thr	Arg	Asn	
Asp	Pro 290	Asp	Gly	Arg	Ser	Arg 295	Leu	Asn	Val	Asn	Val 300	Phe	Thr	Gly	Asn	
Val 305	Ile	Val	Thr	Asp	Phe 310	Gly	Asp	Glu	Thr	Gly 315	Thr	Ile	Ser	Asn	Ile 320	
Gln	Lys	Asp	Lys	Leu 325	Thr	Asp	Val	Phe	Asp 330	Lys	Trp	Leu	Ser	Ser 335	Asp	
Leu	Ala	Lys	Ser 340	Leu	Asn	Cys	His	Cys 345	Ser	Glu	Phe	Ser	Cys 350	Leu	Gly	
Pro	Asn	Val 355	Leu	Val	Lys	Asn	Met 360	Tyr	Tyr	Pro	Asn	Met 365	Asp	Phe	Lys	
Asp	Asn 370	Glu	Arg	His	Met	His 375	Lys	Gln	Pro	Gln	Ile 380	Ile	Gln	Phe		
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<220)>															
	> CD	s														
<222			. (59	5)												
	> RX															
	> 63															
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tttc	tago	ac c	aaaa	caaa	a ct	ctcc	ctag	tat	gggg	tcc	atg	gct	aaa	aca	cat	13

15 Met Ala Lys Thr His

ttt caa ggc aac gaa act gct acc tcc ggc gaa ctg cca cag gtc ggc Phe Gln Gly Asn Glu Thr Ala Thr Ser Gly Glu Leu Pro Gln Val Gly 10 15 20163

-	aac Asn		_					_	. Asn		-	-		Glu	_	211
	tca Ser		Asp					Lys					Ile			259
	gtt Val 55	-			-	_	Ala			-	-	_				307
	gca Ala										Cys					355
	cca Pro															403
	acc Thr															451
atc Ile	gtg Val	ctc Leu 120	gaa Glu	ggc Gly	tca Ser	cca Pro	ctt Leu 125	aag Lys	ggt Gly	ctt Leu	ctt Leu	gca Ala 130	cgc Arg	agc Ser	gtc Val	499
	gtc Val 135															. 547
	atc Ile															595
taat	ttac	tt c	gctc	aggg	ıg aa	t										618
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)> 64 Ala		Thr	His	Phe	Gln	Glv	Asn	Glu	Thr	Ala	Thr	Ser	Glv	Glu	
1				5					10					15		
Leu	Pro	Gln	Val 20	Gly .	Asp :	Asn	Leu	Ala 25	Glu	Phe	Asn	Leu	Val 30	Asn	Thr	
Glu	Leu	Gly 35	Glu '	Val :	Ser :	Ser :	Lys 40	Asp	Phe	Gln	Gly	Arg 45	Lys	Leu	Val	
Leu	Asn 50	Ile	Phe i	Pro	Ser V	/al / 55	Asp	Thr	Gly	Val	Cys . 60	Ala	Thr	Ser	Val	

Arg Lys Phe Asn Glu Ala Ala Ser Leu Glu Asn Thr Thr Val Leu 65 70 75 Cys Ile Ser Lys Asp Leu Pro Phe Ala Leu Gly Arg Phe Cys Ser Ala Glu Gly Ile Glu Asn Val Thr Pro Val Ser Ala Phe Arg Ser Thr Phe Gly Glu Asp Asn Gly Ile Val Leu Glu Gly Ser Pro Leu Lys Gly Leu 120 Leu Ala Arg Ser Val Ile Val Val Asp Glu Asn Gly Lys Val Ala Tyr Thr Gln Leu Val Asp Glu Ile Phe Thr Glu Pro Asp Tyr Asp Ala Ala 150 155 Leu Ala Gly Leu Asn <210> 65 <211> 879 <212> DNA <213> Corynebacterium glutamicum <220> <221> CDS <222> (101)..(856) <223> RXN01676 <400> 65 agttacagct tttctcggtg gcacactcqc gctacttagc ccttgtgccg cactcctttt 60 accagcattt tttgcatcct cagtgggtgc tggcccgcgc atg atc ctt cac ggt Met Ile Leu His Gly gtt gtg ttc tac gca gga ctt cta gta ctt ctc gtg cca ctt ggc ctt 163 Val Val Phe Tyr Ala Gly Leu Leu Val Leu Val Pro Leu Gly Leu 10 15 ggt gcg gga atc ctc ggc gag ctg ttt atc acc caa cgc cag acc atc 211 Gly Ala Gly Ile Leu Gly Glu Leu Phe Ile Thr Gln Arg Gln Thr Ile 30 atc gtg gtt tca tcg atc gtg ctg att atc cta ggt ttt gtc cag atc 259 Ile Val Val Ser Ser Ile Val Leu Ile Ile Leu Gly Phe Val Gln Ile ttc ggc ggc gga ttc gac ttc gga aaa gca ctc cca gga tta gat cgt 307 Phe Gly Gly Gly Phe Asp Phe Gly Lys Ala Leu Pro Gly Leu Asp Arg ctg caa tot aag goo act gtg acc toa ggt ota gga aag ago ttt tta 355 Leu Gln Ser Lys Ala Thr Val Thr Ser Gly Leu Gly Lys Ser Phe Leu

70		7	5				80					85	
cta gga Leu Gly	-			_			-						403
ggc gcc Gly Ala		Thr Le											451
gca ctc Ala Leu													499
gct att Ala Ile 135													547
ctc cgc Leu Arg 150			e Thr										595
tct gtc Ser Val	_		_			-	_						643
tcc acg Ser Thr													691
cag atc			-										739
gac atc o Asp Ile 2 215			-	-	-		_		_				787
aac aaa d Asn Lys i 230	_		Lys	_	_	Ăla	-	-			-	_	835
gga tgg q Gly Trp \	Val Ile			taat	tatt	ag t	tttg	gago	g ag	g			879
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Val Pro Leu Gly Leu Gly Ala Gly Ile Leu Gly Glu Leu Phe Ile Thr

20 25 30

Gln Arg Gln Thr Ile Ile Val Val Ser Ser Ile Val Leu Ile Ile Leu 35 40 45

- Gly Phe Val Gln Ile Phe Gly Gly Phe Asp Phe Gly Lys Ala Leu
 50 55 60
- Pro Gly Leu Asp Arg Leu Gln Ser Lys Ala Thr Val Thr Ser Gly Leu 65 70 75 80
- Gly Lys Ser Phe Leu Leu Gly Met Thr Ser Ser Ile Ala Gly Phe Cys 85 90 95
- Ser Gly Pro Ile Leu Gly Ala Val Leu Thr Leu Ala Ala Thr Ser Gly
 100 105 110
- Asn Ser Ile Thr Ser Ala Leu Ile Leu Ser Ala Tyr Gly Ala Gly Met 115 120 125
- Val Leu Pro Leu Met Ala Ile Ala Ala Leu Trp Ala Lys Leu Gly Gln 130 135 140
- Arg Gly Gln Gln Met Leu Arg Gly Arg Glu Phe Thr Phe Leu Gly Arg 145 150 155 160
- Gln Trp His Ile Val Ser Val Ile Ser Gly Ala Leu Ile Ile Ala Val 165 170 175
- Gly Ile Leu Phe Trp Ser Thr Asn Gly Leu Val Ser Met Pro Glu Leu 180 185 190
- Val Pro Met Asp Thr Gln Ile Trp Leu Gln Glu Ala Thr Phe Ser Leu 195 200 205
- Gly Ser Pro Leu Phe Asp Ile Ala Leu Ile Ile Val Ala Ala Gly Leu 210 215 220
- Phe Leu Tyr Phe Trp Asn Lys Arg Gln Lys Arg Lys Glu Glu Ala Gln 225 230 235 240
- Arg Pro Lys Glu Ser Gly Trp Val Ile Asn Pro Arg 245 250
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- <211> 744
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- <221> CDS
- <222> (101)..(721)
- <223> RXN00380
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cta Leu	gca Ala	gca Ala	aca Thr	atc Ile 10	Gly	tgc Cys	gtg Val	aca Thr	ctc Leu 15	agc Ser	gga Gly	ctt Leu	gcg Ala	cta Leu 20	gta Val	163
				Asp						gac Asp						211
gga Gly	acc Thr	ttc Phe 40	caa Gln	ttc Phe	cac His	tcc Ser	ccg Pro 45	gat Asp	gga Gly	aag Lys	atg Met	gaa Glu 50	att Ile	ttc Phe	tac Tyr	259
		Ala								att Ile						307
										gat Asp 80						355
										gca Ala						403
										ctc Leu						451
										atc Ile						499
	-	-		-		-		_		gac Asp				-		547
	-	Ile	Tyr	Asp	Pro	Pro	Phe	Met	Thr	gca Ala 160	Āla					595
										gtg Val						643
										acc Thr						691
		gcg Ala 200				Val				taaa	tgtc	tg a	gatt	gtgg	ŗt	741

agc 744

<210> 68

<211> 207

<212> PRT

<213> Corynebacterium glutamicum

<400> 68

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Gly Leu Ala Leu Val Ala Cys Ser Ser Asp Ser Thr Ala Gly Thr Asp
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Ala Val Ala Val Gly Gly Thr Phe Gln Phe His Ser Pro Asp Gly Lys
35 40 45

Met Glu Ile Phe Tyr Asp Glu Ala Asp Arg Gln Gln Leu Pro Asp Ile 50 55 60

Gly Gly Asp Ser Leu Met Glu Glu Gly Thr Gln Ile Asn Leu Ser Asp 65 70 75 80

Phe Glu Asn Gln Val Val Ile Leu Asn Ala Trp Gly Gln Trp Cys Ala 85 90 95

Pro Cys Arg Ser Glu Ser Asp Asp Leu Gln Ile Ile His Glu Glu Leu 100 105 110

Gln Ala Ala Gly Asn Gly Asp Thr Pro Gly Gly Thr Val Leu Gly Ile 115 120 125

Asn Val Arg Asp Tyr Ser Arg Asp Ile Ala Gln Asp Phe Val Thr Asp 130 135 140

Asn Gly Leu Asp Tyr Pro Ser Ile Tyr Asp Pro Pro Phe Met Thr Ala 145 150 155 160

Ala Ser Leu Gly Gly Val Pro Ala Ser Val Ile Pro Thr Thr Ile Val 165 170 175

Leu Asp Lys Gln His Arg Pro Ala Ala Val Phe Leu Arg Glu Val Thr 180 185 190

Ser Lys Asp Val Leu Asp Val Ala Leu Pro Leu Val Asp Glu Ala 195 200 205

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gta Val	acc Thr	gaa Glu	gaa Glu	aca Thr 10	Phe	gag Glu	agc Ser	aca Thr	gtt Val 15	acc Thr	ggc	gac Asp	gga Gly	att Ile 20	gtc Val	163
ctc Leu	gta Val	gac Asp	gca Ala 25	tgg Trp	gca Ala	tcc Ser	tgg Trp	tgc Cys 30	gga Gly	cct Pro	tgc Cys	cgc Arg	cag Gln 35	ttc Phe	gcc Ala	211
cca Pro	acc Thr	tac Tyr 40	gag Glu	aag Lys	gtt Val	tcc Ser	gaa Glu 45	acc Thr	cac His	acc Thr	gac Asp	gca Ala 50	acc Thr	ttc Phe	gcc Ala	259
											gca Ala 65					307
cag Gln 70	tcc Ser	atc Ile	cca Pro	act Thr	ctg Leu 75	atg Met	gtt Val	ttc Phe	cgc Arg	gac Asp 80	ggc Gly	atc Ile	atg Met	gtc Val	tac Tyr 85	355
cgc Arg	gaa Glu	gcc Ala	ggc Gly	acc Thr 90	atg Met	cca Pro	gct Ala	cct Pro	gca Ala 95	ctg Leu	gat Asp	gat Asp	ctg Leu	gtc Val 100	aac Asn	403
cag Gln	gtt Val	aag Lys	gca Ala 105	ctc Leu	gac Asp	atg Met	gat Asp	gac Asp 110	gtt Val	cgt Arg	cgc Arg	cag Gln	gtc Val 115	gca Ala	gag Glu	451
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Gly Asp Gly Ile Val Leu Val Asp Ala Trp Ala Ser Trp Cys Gly Pro $20 \\ 25 \\ 30$

Cys Arg Gln Phe Ala Pro Thr Tyr Glu Lys Val Ser Glu Thr His Thr 35 40 45

Asp Ala Thr Phe Ala Lys Leu Asp Thr Glu Ala Asn Gln Gly Leu Ala 55 Ala Ala Leu Gln Ile Gln Ser Ile Pro Thr Leu Met Val Phe Arg Asp Gly Ile Met Val Tyr Arg Glu Ala Gly Thr Met Pro Ala Pro Ala Leu Asp Asp Leu Val Asn Gln Val Lys Ala Leu Asp Met Asp Asp Val Arq 105 Arg Gln Val Ala Glu Gln Gln Gly Ser Ala Glu Ala 120 <210> 71 <211> 990 <212> DNA <213> Corynebacterium glutamicum <220> <221> CDS <222> (101)..(967) <223> RXN02325 <400> 71 cagagatttg aagatggaga ccaaggctca aagggaatcc atgccgtctt ggtttaatac 60 tgcacccgtc taatgaaaat cattactatt aggtgtcatg atg gac cat gca cac 115 Met Asp His Ala His gat too tgo toa coa act ctg cgc cgt gat ttg gag gtc act ggc cag 163 Asp Ser Cys Ser Pro Thr Leu Arg Arg Asp Leu Glu Val Thr Gly Gln 10 15 ctc caa cct gag aaa gct gtc gat tta gca gcg ccg cac gaa ggg aag 211 Leu Gln Pro Glu Lys Ala Val Asp Leu Ala Ala Pro His Glu Gly Lys gtt gcc aat ata acg aag gtg acc tcc tca aat atg gag cac acc atc 259 Val Ala Asn Ile Thr Lys Val Thr Ser Ser Asn Met Glu His Thr Ile 40 acg cag gcc tca aaa gct aag gag gtg gtg gtg ctc att ggt cac tcc Thr Gln Ala Ser Lys Ala Lys Glu Val Val Leu Ile Gly His Ser 60 ctg ccc aca ttt cag gat ttg gaa aaa gac att ctg cac ttt cag 355 Leu Leu Pro Thr Phe Gln Asp Leu Glu Lys Asp Ile Leu His Phe Gln 80 gca ggt aat aaa ggg cga ttt tct gta gcg att gtt gat cct gat cgc 403 Ala Gly Asn Lys Gly Arg Phe Ser Val Ala Ile Val Asp Pro Asp Arg 90 95

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					caa Gln											547
					gag Glu 155											595
_			-		gaa Glu	_			-		_		-			643
					cag Gln											691
					gta Val											739
	-	_			aag Lys	_	_		-		_	-			_	787
					gat Asp 235											835
					gca Ala											883
					ctg Leu											931
ttg Leu	gaa Glu	atc Ile 280	agg Arg	gcg Ala	cag Gln	gtg Val	ggg Gly 285	aat Asn	gca Ala	atg Met	agc Ser	taag	aaaa	ca		977
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- Glu Val Thr Gly Gln Leu Gln Pro Glu Lys Ala Val Asp Leu Ala Ala 20 25 30
- Pro His Glu Gly Lys Val Ala Asn Ile Thr Lys Val Thr Ser Ser Asn 35 40 45
- Met Glu His Thr Ile Thr Gln Ala Ser Lys Ala Lys Glu Val Val Val 50 55 60
- Leu Ile Gly His Ser Leu Leu Pro Thr Phe Gln Asp Leu Glu Lys Asp 65 70 75 80
- Ile Leu His Phe Gln Ala Gly Asn Lys Gly Arg Phe Ser Val Ala Ile 85 90 95
- Val Asp Pro Asp Arg Ser Ala Asp Val Val Ala Arg Phe Arg Pro Lys 100 105 110
- Gln Ile Pro Val Ala Tyr Val Val Lys Asp Gly Ala Ser Ile Ala Glu 115 120 125
- Phe Asn Ser Leu Asn Lys Glu Pro Val Ala Gln Trp Leu Asp His Phe 130 135 140
- Val Ser Arg Glu Thr Ile Pro Asn Glu Lys Glu Gly Asp Val Asp Lys 145 150 155 160
- Gln Ile Asp Pro Arg Leu Trp Arg Ala Ala Glu Leu Val Asn Ala Gly 165 170 175
- Asp Phe Arg Ala Ala Leu Ala Leu Tyr Glu Gln Leu Pro Gln Asp Ala 180 185 190
- Thr Val Lys Arg Ala His Ala Ala Val Ser Val Leu Ala Arg Met Ser . 195 200 205
- Val Ala Asp Arg Gly Glu Asp Pro Ile Glu Lys Ser Arg Arg Asp Pro 210 215 220
- Asp Asp Val Asn Lys Ala Leu Ala Ala Ala Asp Met Tyr Val Leu Met 225 235 240
- Asn Gln Pro Asp Thr Ala Leu Ala His Leu Ala Ala Leu Leu Pro Lys 245 250 255
- Pro Glu Ala Ala Arg Arg Ile Val Glu Leu Leu Asn Leu Phe Asp Pro 260 265 270
- Leu Asp Leu Val Ala Leu Glu Ile Arg Ala Gln Val Gly Asn Ala Met 275 280 285

Ser

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				Ser					Tyr					Ala	act Thr	691
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	_	Gly	_	_						_					cga Arg	787
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					cct Pro											877
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Ile Gly Met Glu Leu Asp Arg Ser Val Ser Pro Cys Thr Val Asn Ala Val Glu His Met Ala Ser Glu Gly Tyr Tyr Asn Asp Thr Val Cys His Arg Ile Thr Thr Ser Gly Ile Tyr Val Leu Gln Cys Gly Asp Pro Ser Ser Thr Gly Ala Gly Gly Pro Gly Phe Ser Phe Ala Asn Glu Tyr Pro Thr Asp Glu Ala Thr Asp Leu Thr Thr Pro Val Ile Tyr Glu Arg Gly 200 Thr Ile Ala Met Ala Asn Ala Gly Ala Asp Thr Asn Gly Leu Pro Val 215 Leu Pro Gln Leu Arg Gly Phe Pro Thr Gly Thr Glu Leu His Leu Leu 235 Arg Pro Asp His Arg Arg Pro Cys Asn Pro Arg Arg His Arg Arg Ser Trp His <210> 75 <211> 741 <212> DNA <213> Corynebacterium glutamicum <220> <221> CDS <222> (1)..(741) <223> RXN01926 <400> 75 ctg cga agc ttc tac acc cca gaa caa gcc atc gaa cgc gaa ggc gac 48 Leu Arg Ser Phe Tyr Thr Pro Glu Gln Ala Ile Glu Arg Glu Gly Asp 5 gtc tgg aaa gcc gcc acc gaa gaa gca gaa ctc ctc gca gct gac ggc · Val Trp Lys Ala Ala Thr Glu Glu Ala Glu Leu Leu Ala Ala Asp Gly 20 25 gcc gtc cac gac cag gaa ctc ttc ctc aac tgc acc acc tcc cca ctg Ala Val His Asp Gln Glu Leu Phe Leu Asn Cys Thr Thr Ser Pro Leu 35 atc ttc gcc tcc gcg atg ctc aac ttc ggc gtc cac caa atc ctg gac 192 Ile Phe Ala Ser Ala Met Leu Asn Phe Gly Val His Gln Ile Leu Asp 50 60 acc etc tgc caa etc gca cca tcc ecc gcc ggc egc gac gca gac ecc 240

Thr 65	Leu	Cys	Gln	Leu	Ala 70	Pro	Ser	Pro	Ala	Gly 75	Arg	Asp	Ala	Asp	Pro 80	
aaa Lys	gcc Ala	ctc Leu	gaa Glu	gcc Ala 85	gcc Ala	acc Thr	tcc Ser	gca Ala	atg Met 90	gac Asp	gac Asp	cac His	cgc Arg	gac Asp 95	acc Thr	288
														atg Met		336
														ggc Gly		384
														agc Ser		432
														acc Thr		480
_		_				_		-			_		_	ggc Gly 175	_	528
	_			_				_		_				tac Tyr	cca Pro	576
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Ile Phe Ala Ser Ala Met Leu Asn Phe Gly Val His Gln Ile Leu Asp 50 60

Thr Leu Cys Gln Leu Ala Pro Ser Pro Ala Gly Arg Asp Ala Asp Pro 65 70 75 80

Lys-Ala Leu Glu Ala Ala Thr Ser Ala Met Asp Asp His Arg Asp Thr 85 90 95

Thr Asp Asp Phe Ser Gly Val Val Phe Lys Val Gln Ala Gly Met Asp 100 105 110

Lys Asn His Arg Asp Thr Leu Ala Phe Met Arg Val Val Ser Gly Glu 115 120 125

Phe Asp Arg Gly Met Gln Val Thr His Ser Gln Ser Gly Arg Ser Phe 130 140

Ser Thr Lys Tyr Ala Leu Thr Val Phe Gly Arg Thr Arg Ser Thr Val 145 150 155 160

Glu Thr Ala Phe Pro Gly Asp Ile Val Gly Leu Val Asn Ala Gly Ala 165 170 175

Leu Ala Pro Gly Asp Thr Ile Phe Glu Gly Arg Lys Ile Gln Tyr Pro 180 185 190

Pro Met Pro Lys Phe Ala Pro Glu His Phe Arg Ile Leu Arg Ala Lys 195 200 205

Ser Leu Gly Lys Tyr Lys Gln Phe Arg Lys Ala Leu Glu Gln Leu Asp 210 215 220

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Met Glu Lys Asp Arg Gly Ile Ser Ile Ala Ser Ser Ala Leu Gln Phe 70 75 65 Glu Tyr Ala Pro Glu Gly His Ala Gly Glu Pro Phe Met Ile Asn Leu Val Asp Thr Pro Gly His Ala Asp Phe Ser Glu Asp Thr Tyr Arg Val Leu Met Ala Val Asp Ala Ala Val Met Leu Met His Ser Val 120 <210> 79 <211> 1080 <212> DNA <213> Corynebacterium glutamicum <220> <221> CDS <222> (101)..(1057) <223> RXN02736 caqaqqatta cccaqcqqqt acqtqqqqtc caaaqaqcqc tqatqaaatq ctttcccqca 60 acgqtcacac ctggcgcagg ccataattta ggggcaaaaa atg atc ttt gaa ctt Met Ile Phe Glu Leu 1 ccq gat acc acc cag caa att tcc aag acc cta act cga ctg cgt 163 Pro Asp Thr Thr Gln Gln Ile Ser Lys Thr Leu Thr Arg Leu Arg 10 15 211 gaa tog ggc acc cag gtc acc acc ggc cga gtg ctc acc ctc atc gtg Glu Ser Gly Thr Gln Val Thr Thr Gly Arg Val Leu Thr Leu Ile Val 25 gtc act gac tcc gaa agc gat gtc gct gca gtt acc gag tcc acc aat 259 Val Thr Asp Ser Glu Ser Asp Val Ala Ala Val Thr Glu Ser Thr Asn 40 gaa ged teg ege gag cac eea tet ege gtg ate att ttg gtg gtt gge 307 Glu Ala Ser Arg Glu His Pro Ser Arg Val Ile Ile Leu Val Val Gly 55 60 gat aaa act gca gaa aac aaa gtt gac gca gaa gtc cgt atc ggt ggc 355 Asp Lys Thr Ala Glu Asn Lys Val Asp Ala Glu Val Arg Ile Gly Gly 70 75 80 gac gct ggt gct tcc gag atg atc atc atg cat ctc aac gga cct gtc Asp Ala Gly Ala Ser Glu Met Ile Ile Met His Leu Asn Gly Pro Val 90 gct gac aag ctc cag tat gtc gtc aca cca ctg ttg ctt cct gac acc Ala Asp Lys Leu Gln Tyr Val Val Thr Pro Leu Leu Pro Asp Thr 105 115

		_	Ala		tgg Trp			Glu			-				_	499
					ato Ile		Gln									547
					cta Leu 155						Asn					595
_		_	-	_	tgg Trp		-			_					_	643
_			-		cac His				_	-						691
					ggc Gly											739
-				_	aaa Lys					_				-	_	787
					gat Asp 235						-	_	_		_	835
_	-			_	cgc Arg				-							883
					cag Gln											931
				Ile	ggt Gly	Arg	Arg	Ser								979
gag Glu	ctt Leu 295	cgc Arg	cac His	atg Met	gat Asp	cca Pro 300	gat Asp	ttg Leu	ggc Gly	tac Tyr	cag Gln 305	cac His	gca Ala	cta Leu	tcc Ser	1027
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tgg																1080

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- <212> PRT
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 35 40 45
- Thr Glu Ser Thr Asn Glu Ala Ser Arg Glu His Pro Ser Arg Val Ile 50 55 60
- Ile Leu Val Val Gly Asp Lys Thr Ala Glu Asn Lys Val Asp Ala Glu 65 70 75 80
- Val Arg Ile Gly Gly Asp Ala Gly Ala Ser Glu Met Ile Ile Met His 85 90 95
- Leu Asn Gly Pro Val Ala Asp Lys Leu Gln Tyr Val Val Thr Pro Leu 100 105 110
- Leu Leu Pro Asp Thr Pro Ile Val Ala Trp Trp Pro Gly Glu Ser Pro 115 120 125
- Lys Asn Pro Ser Gln Asp Pro Ile Gly Arg Ile Ala Gln Arg Arg Ile 130 135 140
- Thr Asp Ala Leu Tyr Asp Arg Asp Asp Ala Leu Glu Asp Arg Val Glu 145 150 155 160
- Asn Tyr His Pro Gly Asp Thr Asp Met Thr Trp Ala Arg Leu Thr Gln 165 170 175
- Trp Arg Gly Leu Val Ala Ser Ser Leu Asp His Pro Pro His Ser Glu 180 185 190
- Ile Thr Ser Val Arg Leu Thr Gly Ala Ser Gly Ser Thr Ser Val Asp 195 200 205
- Leu Ala Ala Gly Trp Leu Ala Arg Arg Leu Lys Val Pro Val Ile Arg 210 215 220
- Glu Val Thr Asp Ala Pro Thr Val Pro Thr Asp Glu Phe Gly Thr Pro 225 230 235 240
- Leu Leu Ala Ile Gln Arg Leu Glu Ile Val Arg Thr Thr Gly Ser Ile 245 250 255
- Ile Ile Thr Ile Tyr Asp Ala His Thr Leu Gln Val Glu Met Pro Glu 260 265 270
- Ser Gly Asn Ala Pro Ser Leu Val Ala Ile Gly Arg Arg Ser Glu Ser

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Phe Ile Ala Pro Asn Asp Gly Ser Ala Asp Leu Phe Val His Tyr Ser 20 25 30

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ccg 504

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<400> 86

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20 25 30

Leu Pro Lys Gly Val Thr Glu Leu His Lys Gly Gln Arg Ile Asp Phe 35 40 45

Asp Phe Ala Ala Gly Arg Lys Gly Pro Gln Ala Leu Arg Ile Lys Ile 50 55 60

Leu Glu Thr Pro Arg Arg Pro Gln His Lys Tyr Lys Pro Glu Glu 65 70 75 80

Leu Asn Gly Met Ile Ser Asp Leu Ile Thr Leu Leu Glu Ser Gly Val 85 90 95

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Gln Val Ala Glu Ile Leu Arg Val Val Ala Lys Glu Leu Glu Ser 115 120 125

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Met Ala Gln Gly Thr

1

gtt aag tgg ttc aac cca gag aag ggc ttc ggc ttc atc gct cct tcc 163 Val Lys Trp Phe Asn Pro Glu Lys Gly Phe Gly Phe Ile Ala Pro Ser 10 15 20

		tcc Ser							Tyr							211
		cgt Arg 40														259
		gct Ala														301
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)> 88	3 Gln	C) w	Thr	V-1	Tue	Trn	Dho	λαη	Dro	Clu	T 110	C1	Pho	C1	
1	NIG	GIII	GLY	5		БуЗ	пр	rne	10	FIU	GIU	nys	GIY	15	GIY	
Phe	Ile	Ala	Pro 20	Ser	Asp	Gly	Ser	Ala 25	Asp	Val	Phe	Val	His 30	Tyr	Ser	
Glu	Ile	Glu 35	Gly	Asn	Gly	Phe	Arg 40	Thr	Leu	Glu	Glu	Asn 45	Gln	Leu	Val	
Glu	Phe 50	Glu	Ile	Gly	Glu	Gly 55	Ala	Lys	Gly	Leu	Gln 60	Ala	Gln	Ala	Val	
Arg 65	Ala	Ile														
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ccg Pro																163

PCT												4	1/0080	VO 0:	'	
		20					15)	10				
	-	Asn		caa Gln			Gly			-	-	Gly				
			Ğlu	gcc Ala 50				Āla					Ile			
				gga Gly										His		
u	-			gaa Glu		-				_	_	_			Glu	_
_		-		ttg Leu		-	_	_			-					
a 4!	gac Asp	gcg Ala	gtt Val 115	tgg Trp	gct Ala	cca Pro	ctt Leu	cta Leu 110	gct Ala	gag Glu	gcc Ala	att	acc Thr 105	atg Met	agt Ser	gcc Ala
			Val	tct Ser 130												
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			-	gct Ala				-		-				-		
: 64 I	gct Ala	tgg Trp 180	gag Glu	cat His	aat Asn	cct Pro	tct Ser 175	att Ile	gtg Val	gtg Val	att Ile	ctg Leu 170	aag Lys	gac Asp	gag Glu	caa Gln
i 69	ctg Leu	ccg Pro	act Thr 195	gaa Glu	tcg Ser	ttg Leu	gag Glu	cgg Arg 190	ctt Leu	agt Ser	atc Ile	agg Arg	ggt Gly 185	acg Thr	cgc Arg	aat Asn
. 73	tta	gaa	caa	tta	gca	gaa	cga	acc	ggt	tca	ggc	gtc	gaa	agg	gtg	ata

ggt gaa tta gcc ttg cgt gat cat ctt gcg ctc ggc agg ctg ttg agt Gly Glu Leu Ala Leu Arg Asp His Leu Ala Leu Gly Arg Leu Leu Ser 250 gtg cca ttt gaa ggc agt gga gtt act cgt cct ctt aca gct gtg tgg 931 Val Pro Phe Glu Gly Ser Gly Val Thr Arg Pro Leu Thr Ala Val Trp 265 270 275 agt gga ccc cgc aga ttg ccg att cta gcg gga gaa tta gtg tcc atc 979 Ser Gly Pro Arg Arg Leu Pro Ile Leu Ala Gly Glu Leu Val Ser Ile 280 285 gca tcg aac cac atc tgattttgag ccctggctaa cgg 1017 Ala Ser Asn His Ile 295 <210> 90 <211> 298 <212> PRT <213> Corynebacterium glutamicum <400> 90 Met Asp Asn Gly Trp Pro Asn Leu Gln Thr Leu Ala Leu Phe Val Ala Ile Val Glu Glu Gly Ser Leu Gly Ala Gly Ala Arg Lys Val Gly Met Ala Gln Pro Asn Ala Ser Arg Ala Ile Ala Glu Leu Glu Ala Asp Met 40 Lys Ala Glu Leu Leu Val Arg His Pro Arg Gly Ser His Pro Thr Ala Ala Gly Leu Ala Leu Val Glu His Ser Arg Asp Leu Leu Gln Ser Val Gln Glu Phe Thr Glu Trp Val Thr Glu Gly Arg Thr Glu Gln Pro Leu Lys Leu His Val Gly Ala Ser Met Thr Ile Ala Glu Ala Leu Leu Pro 105 Ala Trp Val Ala Asp Met Arg Thr Arg Phe Pro Ala Cys Arg Val Asp Val Ser Val Met Asn Ser Ser Gln Val Ile Glu Ala Val Gln Lys Gly 135 His Leu Gln Leu Gly Phe Ile Glu Thr Pro His Val Pro Val Arq Leu 145 150 His Ala Arg Val Val Gln Glu Asp Lys Leu Ile Val Val Ile Ser Pro 165 170 175

Asn His Glu Trp Ala Asn Arg Thr Gly Arg Ile Ser Leu Arg Glu Leu 185 Ser Glu Thr Pro Leu Ile Val Arg Glu Val Gly Ser Gly Thr Arg Glu 200 Ala Leu Gln Glu Leu Leu Ala Asp Tyr Asp Met Ala Glu Pro Ile Gln Val Leu Asn Ser Asn Ala Ala Val Arg Val Val Glu Ala Gly Ala Gly Pro Ala Val Leu Gly Glu Leu Ala Leu Arg Asp His Leu Ala Leu Gly Arg Leu Leu Ser Val Pro Phe Glu Gly Ser Gly Val Thr Arg Pro 265 Leu Thr Ala Val Trp Ser Gly Pro Arg Arg Leu Pro Ile Leu Ala Gly ·Glu Leu Val Ser Ile Ala Ser Asn His Ile 295 <210> 91 <211> 1214 <212> DNA <213> Corynebacterium glutamicum <220> <221> CDS <222> (1)..(1191) <223> RXA02431 <400> 91 gtg gtg gtg aca ccc cgt cat atc gtt tac tcc gca gcc tcg cgc cgg Val Val Val Thr Pro Arg His Ile Val Tyr Ser Ala Ala Ser Arg Arg 1 5 gtg ttc caa atc gtg gaa aaa cgc gcc gga att gtc gaa cgc ctc agc 96 Val Phe Gln Ile Val Glu Lys Arg Ala Gly Ile Val Glu Arg Leu Ser 20 atc gat gaa ggc ttc atg gaa cca gag gct ctc gtt gga gcc acc cca 144 Ile Asp Glu Gly Phe Met Glu Pro Glu Ala Leu Val Gly Ala Thr Pro 35 gaa gag gtg aaa cag tgg gcg gaa gaa tta cgc gcg gaa att aaa gaa 192 Glu Glu Val Lys Gln Trp Ala Glu Glu Leu Arg Ala Glu Ile Lys Glu 50 55

gtt act ggc tta ccc tcc tcg gtt ggt gct ggc tcc ggt aag cag atc

Val Thr Gly Leu Pro Ser Ser Val Gly Ala Gly Ser Gly Lys Gln Ile

gcc aaa att ggt tca ggc gaa gca aag cca gat ggt gtg ttt gtc gtg

70

65

240

288

Ala	Lys	Ile	Gly	Ser 85	Gly	Glu	Ala	Lys	Pro 90	_	Gly	Val	Phe	Val 95	Val	
				Glr	a cat n His				Asp							336
			Val		cct Pro			Gly					Ser			384
	_	Thr			gat Asp		Āla						-	_	-	432
	_			-	acc Thr 150					_				_	_	480
22		_	_	_	cct Pro		_		_	-		_		_		528
					tat Tyr	_		_							_	576
-	-	_			cga Arg		_	_		-		_				624
	-		_		gcc Ala	-		_	_			-		_	-	672
					tct Ser 230											720
-		-			gag Glu	_		_				_	_			768
					atc Ile											816
					gac Asp	Ile										864
	-			-	ccc Pro	_		_			_					912
		-		_	agt Ser			_	-		-		-	-		960

310 305 315 ttg agt atg tgg tgc gca acg caa gat gtc tac cac cca gaa tat ggc 1008 Leu Ser Met Trp Cys Ala Thr Gln Asp Val Tyr His Pro Glu Tyr Gly 325 cac ggt tgg gta caa ggt gcc ggt cac ggt gtt gta tca gta cgt ttt 1056 His Gly Trp Val Gln Gly Ala Gly His Gly Val Val Ser Val Arg Phe gaa acc cgc agc acc aca aaa ggg cga act aaa agt ttt tcc atg gat 1104 Glu Thr Arg Ser Thr Thr Lys Gly Arg Thr Lys Ser Phe Ser Met Asp 360 gac eeg gac etc ace eeg gea gac eet eta gat agt ttg gat tgg get 1152 Asp Pro Asp Leu Thr Pro Ala Asp Pro Leu Asp Ser Leu Asp Trp Ala 375 gac tgg ttt gct gaa aat ggt gaa acg ggg gat gac gaa tagggtttca 1201 Asp Trp Phe Ala Glu Asn Gly Glu Thr Gly Asp Asp Glu tcgggtttcg ggg 1214 <210> 92 <211> 397 <212> PRT <213> Corynebacterium glutamicum <400> 92 Val Val Val Thr Pro Arg His Ile Val Tyr Ser Ala Ala Ser Arg Arg Val Phe Gln Ile Val Glu Lys Arg Ala Gly Ile Val Glu Arg Leu Ser Ile Asp Glu Gly Phe Met Glu Pro Glu Ala Leu Val Gly Ala Thr Pro Glu Glu Val Lys Gln Trp Ala Glu Glu Leu Arg Ala Glu Ile Lys Glu Val Thr Gly Leu Pro Ser Ser Val Gly Ala Gly Ser Gly Lys Gln Ile 70 Ala Lys Ile Gly Ser Gly Glu Ala Lys Pro Asp Gly Val Phe Val Val Pro Val Asp Lys Gln His Asp Leu Leu Asp Pro Leu Pro Val Gly Ala 100 105 Leu Trp Gly Val Gly Pro Val Thr Gly Ser Lys Leu Ala Ser Met Gly Val Glu Thr Ile Gly Asp Leu Ala Ala Leu Thr Gln Lys Glu Val Glu

Ile Ser Leu Gly Ala Thr Ile Gly Ile Ser Leu Trp Asn Leu Ala Arg 145 150 155 160

- Gly Ile Asp Asp Arg Pro Val Glu Pro Arg Ala Glu Ala Lys Gln Ile 165 170 175
- Ser Gln Glu His Thr Tyr Glu Lys Asp Leu Leu Thr Arg Gln Gln Val 180 185 190
- Asp Ala Ala Ile Ile Arg Ser Ala Glu Gly Ala His Arg Arg Leu Leu 195 200 205
- Lys Asp Gly Arg Gly Ala Arg Thr Val Ser Val Lys Leu Arg Met Ala 210 215 220
- Asp Phe Arg Ile Glu Ser Arg Ser Tyr Thr Leu Ser Tyr Ala Thr Asp 225 230 235 240
- Asp Tyr Ala Thr Leu Glu Ala Thr Ala Phe Arg Leu Ala Arg Tyr Pro 245 250 255
- Gly Glu Val Gly Pro Ile Arg Leu Val Gly Val Ser Phe Ser Gly Leu 260 265 270
- Glu Glu Ser Arg Gln Asp Ile Leu Phe Pro Glu Leu Asp Gln Gln Ile 275 280 285
- Ile Val Pro Pro Ala Pro Asp Thr Asp Tyr Glu Val Gly Val Gln Ser 290 295 300
- Ser Ser Ser Ser Glu Ser Thr Gln Val Glu Ala Pro Gln Asp Val Ala 305 310 315 320
- Leu Ser Met Trp Cys Ala Thr Gln Asp Val Tyr His Pro Glu Tyr Gly
 325 330 335
- His Gly Trp Val Gln Gly Ala Gly His Gly Val Val Ser Val Arg Phe 340 345 350
- Glu Thr Arg Ser Thr Thr Lys Gly Arg Thr Lys Ser Phe Ser Met Asp 355 360 365
- Asp Pro Asp Leu Thr Pro Ala Asp Pro Leu Asp Ser Leu Asp Trp Ala 370 380
- Asp Trp Phe Ala Glu Asn Gly Glu Thr Gly Asp Asp Glu 385 390 395
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- <213> Corynebacterium glutamicum
- <220>
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<400> 93

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- gagcgtattc tttgtgttct ctcacgacag gaatactgct atg gcg atc gag tcc 115

 Met Ala Ile Glu Ser

 1 5
- atc gcg tac acc agt gaa gca ctc tca acc ggc agt ggc cgg ctg ggg 163
 Ile Ala Tyr Thr Ser Glu Ala Leu Ser Thr Gly Ser Gly Arg Leu Gly
 10 15 20
- cat gtg cgc tcc aca gat ggt gcg ctc gaa ttt gaa atg aca ccg cca 211 His Val Arg Ser Thr Asp Gly Ala Leu Glu Phe Glu Met Thr Pro Pro 25
- aag gct ttg ggc gga tcc ggt gaa ggc acc aat cca gaa cag ctg ttc 259 Lys Ala Leu Gly Gly Ser Gly Glu Gly Thr Asn Pro Glu Gln Leu Phe 40 45 50
- gcg gta ggt tac gca gcc tgt ttc cac tct gcc atg cac tct gtc gca 307 Ala Val Gly Tyr Ala Ala Cys Phe His Ser Ala Met His Ser Val Ala 55 60 65
- cgc agc cgc aag atc act ctt gaa gac aca gcg gtt ggt gcc cga gtt 355 Arg Ser Arg Lys Ile Thr Leu Glu Asp Thr Ala Val Gly Ala Arg Val 70 80 85
- agc atc ggg cca aac ggc gct ggt gga ttt gag att gcc gta gaa ctc 403 Ser Ile Gly Pro Asn Gly Ala Gly Gly Phe Glu Ile Ala Val Glu Leu 90 95 100
- gaa gta tcg att cct caa ttg cca caa gca gaa gcc cag gaa ctt gct 451 Glu Val Ser Ile Pro Gln Leu Pro Gln Ala Glu Ala Gln Glu Leu Ala 105 110 115
- gat gcc gcg cac cag gtg tgc ccg tat tcc aac gcc aca cga ggc aat 499 Asp Ala Ala His Gln Val Cys Pro Tyr Ser Asn Ala Thr Arg Gly Asn 120 125 130
- atc tcg gta act gtg tca gtc atc gac gaa gag gct taaaaccaca 545

 Ile Ser Val Thr Val Ser Val Ile Asp Glu Glu Ala
 135 140 145
- ggattaacaa aac 558

<210> 94

<211> 145

<212> PRT

<213> Corynebacterium glutamicum

<400> 94

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		Leu					Thr					. Leu			ttc Phe	307
	Ile					Phe									gga Gly 85	355
		_	-		Thr	-				_		aac Asn	-	_		403
-							_					gat Asp				451
	-	_		_		_					_	act Thr 130	_	_		499
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	-		_			-						aag Lys	_			595
												ggc Gly				643
												aac Asn				691
												atc Ile 210				739
gtc Val	gca Ala 215	gca Ala	ctt Leu	Val	ggt Gly	Val	ttg Leu	gct Ala	aac Asn	Phe	ctg Leu 225	gtg Val	ttc Phe	atg Met	tgg Trp	·787·
												aaa Lys				835
			Leu					Gly				gtc Val				883
		Leu					Ala					gcg Ala				931

			Ile		c gg e Gl			. Val					lle		cgc Arg	979
		ı Met			c tci s Sei		a Trp					Glu				1027
	g Lei				t cca l Pro 315	Ala					Ile					1075
					a ggt o Gly					Gln						1123
				Ala	gtç Val				Thr							1171
-	_	aaa Lys 360	Lys	_	ıttt	tat	tàag	ggca	tt c	cc						1206
	0> 9 1> 3	61								·						
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Gly Val Ser Arg Met Trp Ala Ile Asp Pro Thr Glu Gly Asn Phe Ile 145 150155160

Gln Lys Lys Leu Thr Asp Leu Val Ala Leu Ile Val Leu Leu Leu Ala 165 170 175

Met Gly Val Ala Phe Gly Ile Thr Ala Leu Gly Ala Ser Gly Leu Thr 180 185 190

Lys Asn Leu Leu Asp Phe Val Gly Leu Gly Glu Ile Pro Gly Ile Ser 195 200 205

Tyr Ile Thr Trp Val Val Ala Ala Leu Val Gly Val Leu Ala Asn Phe 210 215 220

Leu Val Phe Met Trp Leu Ile Phe Ser Leu Pro Arg Thr Lys Val Pro 225 230 235 240

Met Lys Pro Gly Leu Gln Ala Ala Leu Leu Gly Ala Ile Gly Phe Glu 245 250 255

Val Val Lys Gln Val Gly Ser Leu Leu Ala Ser Asn Ala Leu Ser Asn 260 265 270

Pro Ala Gly Ala Ala Phe Gly Pro Ile Ile Gly Ile Met Val Val Leu 275 280 285

Tyr Leu Ile Trp Arg Ile Leu Met Tyr Cys Ser Ala Trp Ala Ala Thr 290 295 300

Ser Glu Glu Ala Leu Arg Leu Ala Thr Val Pro Ala Pro Glu Pro Ala 305 310 315 320

Ile Ile Arg Val Arg His Glu Ile Asp Pro Gly Glu Glu Val Ser Gln 325 330 335

Ser Ala Arg Lys Val Gly Ile Gly Val Ala Val Gly Ala Ala Thr Ala 340 345 350

Gly Ala Phe Ala Leu Leu Arg Lys Lys

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<223> RXA00981

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					Leu					Arg				atc Ile 20		163
		_		Glu		_			Met					ttt Phe		211
	-					-		Asn		_			_	ttc Phe	_	259
_	_	His	-							_			_	ttg Leu	-	307
		-	_		-		-	-		_	Lys		_	gag Glu		355
														att Ile 100		403
														atg Met		451
	Asn													atc Ile		499
		_	-				-	_	_					caa Gln		547
														gtc Val		595
atc Ile														aaa Lys 180		643
tac Tyr																691
agt Ser						Pro							taaa	cctc	са	740
gttg	aaac	ca c	tg													75 <u>3</u>

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Asn Tyr Gln Phe Gly Ile Asp Glu Ile Leu Thr Lys Ile Asn Ile Leu 35 40 45

Lys Thr Glu Phe Ser Gln Leu His Glu Tyr Ala Pro Ile Glu His Val 50 55 60

Ser Ser Arg Leu Lys Thr Pro Glu Ser Ile Val Lys Lys Val Ile Arg 65 70 75 80

Lys Gly Asp Glu Leu Ser Leu Ala Ala Ile Lys Asp Thr Val Phe Asp $85 \hspace{1.5cm} 90 \hspace{1.5cm} 95$

Ile Ala Gly Ile Arg Ile Val Cys Ser Phe Leu Lys Asp Ala Tyr Ala 100 105 110

Ile Ala Asp Met Leu Thr Asn Gln Lys Asp Val Thr Val Ile Glu Ala 115 120 125

Lys Asp Tyr Ile Ala Asn Pro Lys Pro Asn Gly Tyr Lys Ser Leu His 130 135 140

Leu Ile Leu Gln Val Pro Val Phe Leu Ser Asn Ser Val Glu Lys Val 145 150 155 160

Asn Val Glu Val Gln Ile Arg Thr Ile Ala Met Asp Phe Trp Ala Ser 165 170 175

Leu Glu His Lys Ile Tyr Tyr Lys Phe Glu Gln Glu Val Pro Gln Ser 180 185 190

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<220>

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120 125 cac gaa ggc cat gaa gaa gta gag ggc acc atg ggt cat tcc gtt gag 547 His Glu Gly His Glu Glu Val Glu Gly Thr Met Gly His Ser Val Glu 140 145 aaa acc cac ctg gtt gac ggc gtt gct ggc att gcc acc ctg cct gaa 595 Lys Thr His Leu Val Asp Gly Val Ala Gly Ile Ala Thr Leu Pro Glu ttc tta aac gat gaa cca aac ctg atc tgg ctg tct cag acc acg ctt 643 Phe Leu Asn Asp Glu Pro Asn Leu Ile Trp Leu Ser Gln Thr Thr Leu

499

691

gaa gtc cag cgc ttt gat aag cag gga ttc cac att ctc ttc atc ggt

Glu Val Gln Arg Phe Asp Lys Gln Gly Phe His Ile Leu Phe Ile Gly

tot gtg gac gag acc atg gag atc qtc cqc qaq ctq aaq qtq aaq ttc

Ser Val Asp Glu Thr Met Glu Ile Val Arg Glu Leu Lys Val Lys Phe

138

185 190 195

cct cag ctg cag gat cca ccg tca gat gat att tgc tac gcc acg cag 739
Pro Gln Leu Gln Asp Pro Pro Ser Asp Asp Ile Cys Tyr Ala Thr Gln
200 205 210

aac cgc cag gtt gcc gtc aag gct atc gct gag cgc tgc gag ctg atg 787 Asn Arg Gln Val Ala Val Lys Ala Ile Ala Glu Arg Cys Glu Leu Met 215 220 225

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gtc gct aag caa aac ggt gcc gat aac gcc tac ctg gtg gat tac gcc 883 Val Ala Lys Gln Asn Gly Ala Asp Asn Ala Tyr Leu Val Asp Tyr Ala 250 255 260

cgc gaa atc gac cca gca tgg ttc gaa ggc gta gag acc atc ggt atc 931 Arg Glu Ile Asp Pro Ala Trp Phe Glu Gly Val Glu Thr Ile Gly Ile 265 270 275

tcc tcc ggc gct tcc gtg cct gag atc ctc gtc cag ggc gtc att gag 979 Ser Ser Gly Ala Ser Val Pro Glu Ile Leu Val Gln Gly Val Ile Glu 280 285 290

cgc ctg gct gag ttc ggc tac gac gtc gag gaa gtc acc tcc gcc 1027 Arg Leu Ala Glu Phe Gly Tyr Asp Asp Val Glu Glu Val Thr Ser Ala 295 300 305

gct gag aag att gtt ttc gcg ctg cct cgc gtg ctg cgc cac aag aat 1075 Ala Glu Lys Ile Val Phe Ala Leu Pro Arg Val Leu Arg His Lys Asn 310 325

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Glu Thr Val Glu Arg Ala Leu Glu Glu Tyr Gly Ala Pro Ile Tyr Val 35 40

Arg Lys Glu Ile Val His Asn Arg Tyr Val Val Asp Thr Leu Ala Glu
50 55 60

Lys Gly Ala Ile Phe Val Asn Glu Ala Ser Glu Ala Pro Glu Gly Ala 65 70 75 80

Asn Met Val Phe Ser Ala His Gly Val Ser Pro Met Val His Glu Glu Ala Ala Lys Asn Ile Lys Ala Ile Asp Ala Ala Cys Pro Leu Val Thr Lys Val His Lys Glu Val Gln Arg Phe Asp Lys Gln Gly Phe His Ile Leu Phe Ile Gly His Glu Gly His Glu Glu Val Glu Gly Thr Met Gly His Ser Val Glu Lys Thr His Leu Val Asp Gly Val Ala Gly Ile 155 Ala Thr Leu Pro Glu Phe Leu Asn Asp Glu Pro Asn Leu Ile Trp Leu 165 170 175 Ser Gln Thr Thr Leu Ser Val Asp Glu Thr Met Glu Ile Val Arg Glu 185 Leu Lys Val Lys Phe Pro Gln Leu Gln Asp Pro Pro Ser Asp Asp Ile Cys Tyr Ala Thr Gln Asn Arg Gln Val Ala Val Lys Ala Ile Ala Glu Arg Cys Glu Leu Met Ile Val Val Gly Ser Arg Asn Ser Ser Asn Ser 235 Val Arg Leu Val Glu Val Ala Lys Gln Asn Gly Ala Asp Asn Ala Tyr Leu Val Asp Tyr Ala Arg Glu Ile Asp Pro Ala Trp Phe Glu Gly Val 260 265 Glu Thr Ile Gly Ile Ser Ser Gly Ala Ser Val Pro Glu Ile Leu Val 280

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							Thr					Ala		ccc Pro		787
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					Leu					Ala				gat Asp 260		883
									Val					ggc		931
													Ile	aaa Lys		979
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cca																1131
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- Gly Glu Ser Ile Pro Thr Thr Ala Ala Arg Glu Ile Leu Glu Glu Thr 85 90 95
- Gly Tyr Asp Ile Arg Leu Gly Lys Leu Ile Gly Lys Val Thr Tyr Pro 100 105 110
- Val Leu Asp Arg Thr Lys Val Val Tyr Tyr Trp Thr Ala Gln Val Leu 115 120 125
- Gly Gly Glu Phe Val Pro Asn Asp Glu Val Asp Glu Ile Arg Trp Leu 130 135 140
- Ser Val Asp Glu Ala Cys Glu Leu Leu Ser Tyr Gln Val Asp Thr Glu 145 150 155 160
- Val Leu Ala Lys Ala Ala Lys Arg Phe Arg Thr Pro Ser Thr Thr Arg 165 170 175
- Val Leu Tyr Val Arg His Ala His Ala His Gly Arg Gln Thr Trp Gly 180 185 190
- Gly Asp Asp Asn Lys Arg Pro Leu Asp Lys Lys Gly Arg Arg Gln Ala 195 200 205
- Glu Met Leu Val Pro Met Leu Leu Pro Phe Lys Pro Thr Ala Ile Tyr 210 215 220
- Ser Ala Val Pro Asp Arg Cys Gln Ala Thr Ala Leu Pro Leu Ala Asp 225 230 235 240
- Glu Leu Gly Leu Asp Val Ser Val Asn Arg Leu Phe Gly Asp Asp Ala 245 250 255
- Trp Glu Thr Asp Pro Glu Ala Cys Lys Lys Arg Phe Thr Asp Val Val 260 265 270
- Ala Gln Gly Gly Val Pro Met Ile Val Gly Gln Gly Asp Ile Ile Pro 275 280 285
- Glu Met Ile Lys Trp Phe Ser Glu Asn Gly Thr Leu Pro Ile Asp Glu 290 295 300
- Lys Ile Lys Ala Lys Lys Gly Ser Val Trp Val Leu Ser Phe His Asp 305 310 315 320
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35 40 45

Leu Asp Arg Arg Gly Arg Leu Leu Trp Ser Met Pro Lys Gly His Val
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Glu Pro Gly Glu Asp Lys Ala Ala Thr Ala Glu Arg Glu Val Trp Glu 65 70 75 80

Glu Thr Gly Ile His Gly Glu Val Phe Thr Glu Leu Gly Val Ile Asp 85 90 95

Tyr Trp Phe Val Ser Glu Gly Lys Arg Ile His Lys Thr Val His His 100 105 110

His Leu Leu Arg Tyr Val Asp Gly Asp Leu Asn Asp Glu Asp Pro Glu 115 120 125

Val Thr Glu Val Ala Trp Ile Pro Ala Asn Gln Leu Ile Glu His Leu 130 135 140

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	Arg					Gli					Pro	tta Leu				355
					Ala					Lev		gca Ala			Ser	403
				Leu					Asp			cat His		Leu		451
			Asp					His				tta Leu 130				499
		-				_	Gln					agc Ser		_		547
											Leu	aat Asn				595
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Acr	Pho	C1.	Dro	720	Val	7	Clu	T ou	W-1	C1	C1	Ton	mh -	T	Cln	

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Leu	His	115		Met	Ser	Ile	Leu 120		Asp	Leu	ı Glu	11e 125		Gl _y	/ Glu	
Asp	Leu 130		Gln	Arg	Phe	Asn 135	Ala	Gly	Lys	Glu	Gln 140		Ile	Trp	Trp	
Tyr 145	Ser	Glu	Val	Tyr	Gln 150	Ile	Ser	Leu	Gln	Arg 155		Gly	Phe	Asr	160	
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					acc (Thr											211
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aac Asn	aaa Lys 55	ctc Leu	acc Thr	tca (Ser i	gca q Ala V	gtc (/al (ggg Gly	gaa (Glu)	gca Ala	gca Ala	gac Asp 65	cta Leu	gcg Ala	aaa Lys	acg Thr	307

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Ser Glu Lys Gly Ile Asn Lys Leu Thr Ser Ala Val Gly Glu Ala Ala 50 60

Asp Leu Ala Lys Thr Leu Gly Cys Ala Glu Leu Met Pro Phe Ala Thr
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Ser Ala Val Arg Ser Ala Thr Asn Ser Glu Ala Val Leu Asp His Val 85 90 95

Glu Lys Glu Thr Gly Val Arg Leu Ser Ile Leu Ser Gly Glu Asp Glu 100 105 110

Ala Arg Gln Thr Phe Leu Ala Val Arg Arg Trp Tyr Gly Trp Ser Ala 115 120 125

Gly Arg Ile Thr Asn Leu Asp Ile Gly Gly Ser Leu Glu Leu Ser 130 135 140

Ser Gly Thr Asp Glu Ser Pro Asp Leu Ala Phe Ser Leu Asp Leu Gly 145 150 155 160

Ala Gly Arg Leu Thr His Asn Trp Phe Asp Thr Asp Pro Pro Ala Arg 165 170 175

Lys Lys Ile Asn Leu Leu Arg Asp Tyr Ile Asp Ala Glu Leu Ala Glu 180 185 190

Pro Ala Arg Gln Met Arg Thr Leu Gly Pro Ala Arg Leu Ala Val Gly 195 200 205

Thr Ser Lys Thr Phe Arg Thr Leu Ala Arg Leu Thr Gly Ala Ala Pro 210 215 220

Ser Ser Ala Gly Pro His Val Thr Arg Thr Leu Thr Ala Pro Gly Leu 225 230 235 240

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atc gac tta gcc tcc aaa gaa gcc ggt gta gac tac atc att att tcc 451 Ile Asp Leu Ala Ser Lys Glu Ala Gly Val Asp Tyr Ile Ile Ser 110 gaa aaa gac atc ctc gac ggc ctc atc ctt ggc ctg gta gaa gcc gac 499 Glu Lys Asp Ile Leu Asp Gly Leu Ile Leu Gly Leu Val Glu Ala Asp 125 534 tct ttg aag aaa taggacccta gttttaaacc act Ser Leu Lys Lys 135 <210> 112 <211> 137 <212> PRT <213> Corynebacterium glutamicum <400> 112 Val Glu Ile Ala Arg Asp Tyr Val Ala Glu Arg Ile Gln Glu Val Lys Ala Ile Val Pro Ile Ser Lys Ala Lys Thr Phe Val Gly Cys Ala Gly Thr Phe Thr Thr Ile Ser Ala Trp Val Gln Gly Leu Glu Ser Tyr Asp Arg Asp Ala Ile His Leu Ser Ala Leu Asn Phe Asp Ala Leu Arg Val Val Thr Asp Glu Ile Ile Ser Glu Ser Ser Ser Gln Arg Ala Ser Asn Pro Val Val Asp Pro Gly Arg Ala Asp Val Ile Gly Gly Gly Ser Val Val Val Gln Ala Ala Ile Asp Leu Ala Ser Lys Glu Ala Gly Val Asp Tyr Ile Ile Ser Glu Lys Asp Ile Leu Asp Gly Leu Ile Leu Gly Leu Val Glu Ala Asp Ser Leu Lys Lys <210> 113 <211> 636 <212> DNA <213> Corynebacterium glutamicum <220> <221> CDS <222> (101)..(613) <223> RXA02159

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	_			_	Glu					Val		_		gca Ala 20	-	163
				Leu										agc Ser		211
_		_	Ser	-	_	_	-	-	_			_		acc Thr	_	259
														gtt Val		307
	-			_	-				-			-	_	agc Ser		355
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211

aag cca ggt acg aaa tta aat caa cag tcc ctt gat tcc att gct gaa

Lys Pro Gly Thr Lys Leu Asn Gln Gln Ser Leu Asp Ser Ile Ala Glu 25 30 35	
gtt ggc gca gat atg tct caa ggg ttt cca aag ggc att gac cag gag Val Gly Ala Asp Met Ser Gln Gly Phe Pro Lys Gly Ile Asp Gln Glu 40 45 50	259
tta att aag cga gta gac cgc gtg gtc att ctt ggt gcc gaa gct caa Leu Ile Lys Arg Val Asp Arg Val Val Ile Leu Gly Ala Glu Ala Gln . 55 60 65	307
cta gaa atg cct atc gat gca aac ggc ata cta cag cgc tgg gta act Leu Glu Met Pro Ile Asp Ala Asn Gly Ile Leu Gln Arg Trp Val Thr 70 75 80 85	355
gac gaa ccc tct gaa cgt gga att gaa ggt atg gaa cgc atg cgc ctg Asp Glu Pro Ser Glu Arg Gly Ile Glu Gly Met Glu Arg Met Arg Leu 90 95 100	403
gtc cga gat gat att gac gcc cga gtc caa aac ctc gtc gct gaa cta Val Arg Asp Asp Ile Asp Ala Arg Val Gln Asn Leu Val Ala Glu Leu 105 110 115	451
acc caa aac gca tagcagtttt ctaatctcac aca Thr Gln Asn Ala 120	486
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ggc	ttgg	acc	aaaa	atct	tt a	aaaa	ggag	a at	gcag	gato		Lys			ttg Leu 5	115
ttt Phe	gtg Val	tgc Cys	gtc Val	ggt Gly 10	aat Asn	ggc Gly	gga Gly	aaa Lys	tca Ser 15	Gln	atg Met	gcg Ala	gcg Ala	gcg Ala 20	ctg Leu	163
				Ala	tca Ser				Glu							211
			Gln		cta Leu											259
gtg Val	ggc Gly 55	gct Ala	gat Asp	atg Met	tcg Ser	caa Gln 60	gga Gly	att Ile	ccc Pro	aaa Lys	gcg Ala 65	atc Ile	gat Asp	ccg Pro	gag Glu	307
ctg Leu 70	ctg Leu	cgc Arg	act Thr	gtc Val	gat Asp 75	cgt Arg	gtg Val	gtt Val	att Ile	ttg Leu 80	ggc Gly	gat Asp	gac Asp	gca Ala	cag Gln 85	355
					tct Ser											403
gag Glu	gaa Glu	ccg Pro	gat Asp 105	gct Ala	caa Gln	ggt Gly	atg Met	gaa Glu 110	cgt Arg	atg Met	cgt Arg	att Ile	gtg Val 115	cgg Arg	gat Asp	451
cag Gln	atc Ile	gat Asp 120	aac Asn	cga Arg	gtc Val	caa Gln	gct Ala 125	ttg Leu	cta Leu	gcg Ala	gga Gly	taaç	geged	ega		497
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<213> Corynebacterium glutamicum

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His Ser Ala Gly Thr Lys Pro Ala Gln Gly Leu Asn Gln Leu Ser Val 35 40 45

Glu Ser Ile Ala Glu Val Gly Ala Asp Met Ser Gln Gly Ile Pro Lys
50 55 60

Ala Ile Asp Pro Glu Leu Leu Arg Thr Val Asp Arg Val Val Ile Leu 65 70 75 80

Gly Asp Asp Ala Gln Val Asp Met Pro Glu Ser Ala Gln Gly Ala Leu 85 90 95

Glu Arg Trp Ser Ile Glu Glu Pro Asp Ala Gln Gly Met Glu Arg Met 100 105 110

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Gly

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Met Ile Glu Gly Trp

ctc atg acc ctt act aaa gag cat tcg aca cct cga gcg gct ggc tca $\,$ 163 Leu Met Thr Leu Thr Lys Glu His Ser Thr Pro Arg Ala Ala Gly Ser $\,$ 10 $\,$ 15 $\,$ 20

atg tcg ttt ctt gac cgc tgg tta gct gcc tgg att ttc ttg gct atg 211 Met Ser Phe Leu Asp Arg Trp Leu Ala Ala Trp Ile Phe Leu Ala Met 25 30 35

gct gct ggg ttg tta atc ggc aag gtc ttt cca gga att ggg gcg ctt 259

Ala Ala Gly Leu Leu Ile Gly Lys Val Phe Pro Gly Ile Gly Ala Leu 40 45 ttg agc gcg gtg gaa att ggt gga att tcc att cca att gct atc ggt 307 Leu Ser Ala Val Glu Ile Gly Gly Ile Ser Ile Pro Ile Ala Ile Gly 55 60 ttg atc gtc atg atg tat cca cct ttg gcc aag gtg cgc tac gac aaa 355 Leu Ile Val Met Met Tyr Pro Pro Leu Ala Lys Val Arg Tyr Asp Lys act aaa gaa atc agc aca gac cgc gct ctc atg gtg gtg tcg att atg 403 Thr Lys Glu Ile Ser Thr Asp Arg Ala Leu Met Val Val Ser Ile Met 90 ttq aac tqq atc qtt qqa cca qca ctt atq ttt aqc ctq qcq tqq ctq 451 Leu Asn Trp Ile Val Gly Pro Ala Leu Met Phe Ser Leu Ala Trp Leu 105 110 ttt ctt cca gat caa cca gag ctt cgc act ggg cta att atc gtg ggc 499 Phe Leu Pro Asp Gln Pro Glu Leu Arg Thr Gly Leu Ile Ile Val Gly 120 125 ctt gcg cgc tgt atc gcg atg gtt ttg gta tgg agt gat ctc gct tgt 547 Leu Ala Arg Cys Ile Ala Met Val Leu Val Trp Ser Asp Leu Ala Cys 135 140 ggt gac cgg gaa gca act gct gtg ctg gtt gca atc aac tcg gtg ttc Gly Asp Arg Glu Ala Thr Ala Val Leu Val Ala Ile Asn Ser Val Phe 150 155 160 cag atc ctt atg ttc ggt gtg ctt ggt tgg ttt tac ctg cag att ctt Gln Ile Leu Met Phe Gly Val Leu Gly Trp Phe Tyr Leu Gln Ile Leu 170 ccc tcg tgg ctg gga tta gac acc acg tcg gtg act ttc tct gtg gta Pro Ser Trp Leu Gly Leu Asp Thr Thr Ser Val Thr Phe Ser Val Val 185 190 tca atc gtg act tcc gtt ctc gtg ttc ttg ggc ata cca ctt gta gct 739 Ser Ile Val Thr Ser Val Leu Val Phe Leu Gly Ile Pro Leu Val Ala 205 gga gtt tta tct cgc gtc att ggt gaa aaa aca aag gga cgg cgc tgg 787 Gly Val Leu Ser Arg Val Ile Gly Glu Lys Thr Lys Gly Arg Arg Trp tac gag gac acg ttc ctg cct aag att tca ccc ttg gcg ctg att ggc 835 Tyr Glu Asp Thr Phe Leu Pro Lys Ile Ser Pro Leu Ala Leu Ile Gly 230 235 240 ttg cta tac aca att gtt ctg ctg ttt tcg ttg cag ggg gat gaa atc 883 Leu Leu Tyr Thr Ile Val Leu Leu Phe Ser Leu Gln Gly Asp Glu Ile 250 255 aca gcg cag cct tgg aca gta gct cgt ctt gca ttg ccg ctg ctg atg 931 Thr Ala Gln Pro Trp Thr Val Ala Arg Leu Ala Leu Pro Leu Leu Met

265 270 275

tac ttt gtg ggc atg ttt ttc att tcc ctg gtg gta tcc aaa ctg tcc 979
Tyr Phe Val Gly Met Phe Phe Ile Ser Leu Val Val Ser Lys Leu Ser
280 285 290

ggg tta act tat gag cga gct gct tcc gtg tct ttt act gca gca gga 1027 Gly Leu Thr Tyr Glu Arg Ala Ala Ser Val Ser Phe Thr Ala Ala Gly 295 300 305

aac aac ttt gaa tta gcg att gcg gta tcg atc gga acc ttt ggt gcg 1075 Asn Asn Phe Glu Leu Ala Ile Ala Val Ser Ile Gly Thr Phe Gly Ala 310 315 320 325

aca tca ccg cag gca tta gct gga acg atc ggc cct ttg att gaa gtc 1123
Thr Ser Pro Gln Ala Leu Ala Gly Thr Ile Gly Pro Leu Ile Glu Val
330 335 340

cca gta tta gtc gga ttg gtt tat gtc atg ttg tgg ctt gga cca aaa 1171 Pro Val Leu Val Gly Leu Val Tyr Val Met Leu Trp Leu Gly Pro Lys 345 350 355

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tgc 1221

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<211> 366

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<213> Corynebacterium glutamicum

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Ile Phe Leu Ala Met Ala Ala Gly Leu Leu Ile Gly Lys Val Phe Pro 35 40 45

Gly Ile Gly Ala Leu Leu Ser Ala Val Glu Ile Gly Gly Ile Ser Ile 50 55 60

Pro Ile Ala Ile Gly Leu Ile Val Met Met Tyr Pro Pro Leu Ala Lys 65 70 75 80

Val Arg Tyr Asp Lys Thr Lys Glu Ile Ser Thr Asp Arg Ala Leu Met
85 90 95

Val Val Ser Ile Met Leu Asn Trp Ile Val Gly Pro Ala Leu Met Phe 100 105 110

Ser Leu Ala Trp Leu Phe Leu Pro Asp Gln Pro Glu Leu Arg Thr Gly

125

15 120

Leu Ile Ile Val Gly Leu Ala Arg Cys Ile Ala Met Val Leu Val Trp 130 135 140

Ser Asp Leu Ala Cys Gly Asp Arg Glu Ala Thr Ala Val Leu Val Ala 145 150 155 160

Ile Asn Ser Val Phe Gln Ile Leu Met Phe Gly Val Leu Gly Trp Phe 165 170 175

Tyr Leu Gl
n Ile Leu Pro Ser Trp Leu Gly Leu Asp Thr Thr Ser Val
 180 \$185 \$190

Thr Phe Ser Val Val Ser Ile Val Thr Ser Val Leu Val Phe Leu Gly 195 200 205

Ile Pro Leu Val Ala Gly Val Leu Ser Arg Val Ile Gly Glu Lys Thr 210 215 220

Lys Gly Arg Arg Trp Tyr Glu Asp Thr Phe Leu Pro Lys Ile Ser Pro 225 230 235 240

Leu Ala Leu Ile Gly Leu Leu Tyr Thr Ile Val Leu Leu Phe Ser Leu 245 250 255

Gln Gly Asp Glu Ile Thr Ala Gln Pro Trp Thr Val Ala Arg Leu Ala 260 265 270

Leu Pro Leu Leu Met Tyr Phe Val Gly Met Phe Phe Ile Ser Leu Val 275 280 285

Val Ser Lys Leu Ser Gly Leu Thr Tyr Glu Arg Ala Ala Ser Val Ser 290 295 300

Phe Thr Ala Ala Gly Asn Asn Phe Glu Leu Ala Ile Ala Val Ser Ile 305 310 315 320

Gly Thr Phe Gly Ala Thr Ser Pro Gln Ala Leu Ala Gly Thr Ile Gly 325 330 335

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Phe	Leu	Gly 200		Pro	Leu	Leu	Ala 205		Va]	Phe	Ser	Arg 210		lle	Gly	
		Ile					Trp					Phe			gca Ala	787
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ttt Phe	tca Ser	ttg Leu	caa Gln	ggt Gly 250	gat Asp	cag Gln	atc Ile	gtc Val	tct Ser 255	Gln	cca Pro	tgg Trp	gct Ala	gta Val 260	gtt Val	883
cgt Arg	ctc Leu	gcg Ala	ata Ile 265	cca Pro	ttg Leu	gtt Val	atc Ile	tat Tyr 270	ttc Phe	gtt Val	gga Gly	atg Met	ttt Phe 275	ttc Phe	att Ile	931
tca Ser	ctc Leu	att Ile 280	gcg Ala	tca Ser	aaa Lys	cta Leu	tct Ser 285	ggc Gly	atg Met	aac Asn	tat Tyr	gca Ala 290	aag Lys	tct Ser	gca Ala	979
tcc Ser	gtc Val 295	tct Ser	ttc Phe	act Thr	gca Ala	gct Ala 300	ggc Gly	aac Asn	aat Asn	ttt Phe	gaa Glu 305	ctt Leu	gcg Ala	att Ile	gcg Ala	1027
														gca Ala		1075
acg Thr	att Ile	ggt Gly	ccc Pro	ttg Leu 330	att Ile	gaa Glu	att Ile	cca Pro	gta Val 335	ctt Leu	gtc Val	ggc Gly	ttg Leu	gtc Val 340	tac Tyr	1123
gcc Ala	atg Met	ctg Leu	tgg Trp 345	cta Leu	ggc Gly	ccc Pro	aag Lys	ttg Leu 350	ttc Phe	cca Pro	aat Asn	gac Asp	ccc Pro 355	acg Thr	ctg Leu	1171
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3

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		120		GIU	1 116	H1S	125		vai	. Leu	Glu	11e 130		ser	GIU	
_		Val				_	Āla		_		ccg Pro 145				_	547
-	Ile	_	-		_	Tyr	_			-	gga Gly	-		_		595
		-			Gly	_				Asp	tgg Trp					643
_		-	-	Gly		_	-		Gln	_	ata Ile					691
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		-			g.											
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Met 1	Thr	Gly	Gln	Ala 5	Ala	Pro	Asn	Leu	10		Asn Val			15		
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Met 1 Ile Thr Ala Asp 65	Thr Ala Ile Lys 50 Arg	Asn Asn 35 Ile	Glu 20 Arg His	Ala 5 Leu Tyr Thr	Ala Ala Ile His Leu 70	Pro Leu Phe Leu 55	Asn Thr Glu 40 Pro	Leu Tyr 25 Ser Ile Ala	10 Gln Tyr Leu Glu	Gly Val Ala Gly 75	Val Ser Glu 60	Phe Leu 45 Gly Val	Ser 30 Ala Phe	15 Ala Arg Ala Ser	Glu Thr Lys Pro	
Met 1 Ile Thr Ala Asp 65 Val	Thr Ala Ile Lys 50 Arg	Asn Asn 35 Ile Leu	Glu 20 Arg His Val	Ala 5 Leu Tyr Thr Ala Leu 85	Ala Ala Ile His Leu 70 Phe	Pro Leu Phe Leu 55 Ala	Asn Thr Glu 40 Pro Val Cys	Leu Tyr 25 Ser Ile Ala Val	10 Gln Tyr Leu Glu His 90	Gly Val Ala Gly 75 Asn	Val Ser Glu 60 Lys	Phe Leu 45 Gly Val	Ser 30 Ala Phe Ala Arg	Ala Arg Ala Ser Ser 95	Glu Thr Lys Pro 80 Gln	
Met 1 Ile Thr Ala Asp 65 Val	Thr Ala Ile Lys 50 Arg Pro	Asn Asn 35 Ile Leu Gln Ser	Gln Glu 20 Arg His Val Ala 100	Ala 5 Leu Tyr Thr Ala Leu 85	Ala Ala Ile His Leu 70 Phe	Pro Leu Phe Leu 55 Ala Ile Ser	Asn Thr Glu 40 Pro Val Cys	Leu Tyr 25 Ser Ile Ala Val Tyr 105	10 Gln Tyr Leu Glu His 90 Ala	Gly Val Ala Gly 75 Asn	Val Ser Glu 60 Lys Ala	Phe Leu 45 Gly Val Gly Ser	Ser 30 Ala Phe Ala Arg Val	Ala Arg Ala Ser Ser 95 Glu	Glu Thr Lys Pro 80 Gln Val	

166

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Gl	у Су	s Gl	y As	р Va 16		s Pro	o Me	t Ty	r Pre		y Ly:	s Hi	з Ту	Let 175	a Asp	
Tr	p Gl	u Le	u Al. 18		p Pro	o Sei	c Ası	Gl:		y Glu	u Ası	p Ly:	190		n Glu	
Il	e Ile	e Glu 199		u Ile	e Asp	Gly	/ Arc		e Aro	g Glu	ı Leı	205	_	Ser	: Ile	
Gli	n Lei 210		c Gli	n Ası	n											
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											gtg	aat Asn	gaa	gag	ata Ile 5	115
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tgg Trp	gta Val	caa Gln	acc Thr 25	att Ile	gtg Val	ctc Leu	tcc Ser	atc Ile 30	gtt Val	caa Gln	ggc	ctc Leu	aca Thr 35	gag Glu	ttc Phe	211
ctg Leu	ccg Pro	atc Ile 40	agc Ser	tcc Ser	agc Ser	gga Gly	cac His 45	ctc Leu	cga Arg	atc Ile	atc Ile	tct Ser 50	gag Glu	ctg Leu	ttc Phe	259
tgg Trp	ggt Gly 55	gcc Ala	gat Asp	gcc Ala	ggc Gly	gcg Ala 60	tcc Ser	ttt Phe	acc Thr	gcc Ala	gtg Val 65	gtt Val	cag Gln	ctt Leu	ggt Gly	307
acc Thr 70	gaa Glu	gcc Ala	gca Ala	gtg Val	ctg Leu 75	gtg Val	ttt Phe	ttt Phe	gcc Ala	aag Lys	gaa Glu	atc Ile	tgg Trp	caa Gln	atc Ile	355

403

atc aca ggt tgg ttc gct ggc gta ttc aat aag gaa cgc cgc gga ttt Ile Thr Gly Trp Phe Ala Gly Val Phe Asn Lys Glu Arg Arg Gly Phe

			•	90)				95	5				100		
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		Ile			tcc Ser		Leu									547
	Ala				ggc Gly 155											595
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cct Pro	ggc Gly	gtg Val	tct Ser 185	cgc Arg	tcc Ser	ggc Gly	ggc Gly	acc Thr 190	atc Ile	tct Ser	gct Ala	ggt Gly	ttg Leu 195	ttc Phe	ctt Leu	691
					gta Val											739
cct Pro	gca Ala 215	gtg Val	ctt Leu	ggc Gly	tcc Ser	ggt Gly 220	ttg Leu	tac Tyr	tcc Ser	ctg Leu	cct Pro 225	gac Asp	gct Ala	ttt Phe	gcg Ala	787
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- Ile Ser Glu Leu Phe Trp Gly Ala Asp Ala Gly Ala Ser Phe Thr Ala
 50 55 60
- Val Val Gln Leu Gly Thr Glu Ala Ala Val Leu Val Phe Phe Ala Lys 65 70 75 80
- Glu Ile Trp Gln Ile Ile Thr Gly Trp Phe Ala Gly Val Phe Asn Lys 85 90 95
- Glu Arg Arg Gly Phe Glu Tyr Arg Met Gly Trp Met Ile Ile Val Ala 100 105 110
- Thr Ile Pro Val Val Ile Leu Gly Val Leu Gly Lys Asp Leu Ile Arg 115 120 125
- Glu Ala Leu Arg Asn Met Trp Ile Thr Ala Ser Val Leu Ile Leu Phe 130 135 140
- Ser Leu Val Phe Ile Leu Ala Glu Lys Met Gly Lys Lys Glu Arg Asp 145 150 155 160
- Tyr Asp Lys Leu Thr Met Lys Asp Ala Ile Ile Met Gly Leu Ala Gln 165 170 175
- Cys Leu Ala Leu Ile Pro Gly Val Ser Arg Ser Gly Gly Thr Ile Ser 180 185 190
- Ala Gly Leu Phe Leu Gly Leu Lys Arg Glu Val Ala Thr Lys Phe Ser 195 200 205
- Phe Leu Leu Ala Ile Pro Ala Val Leu Gly Ser Gly Leu Tyr Ser Leu 210 215 220
- Pro Asp Ala Phe Ala Pro Ser Ser Gly Gln Ala Ala Ser Gly Leu Gln 225 230 235 240
- Leu Thr Val Gly Thr Leu Val Ala Phe Val Val Gly Tyr Ile Ser Ile 245 250 255
- Ala Trp Leu Met Lys Phe Val Ala Asn His Ser Phe Ser Trp Phe Ala 260 265 270
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290

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tag	tgat	cgc	acgo	cctg	gtg d	aggo	gctt	g go	ggc	ggtgd		. Arc			gcg Ala 5	115
cgc Arg	gcg	ato Ile	gto Val	g cca Pro	Asp	ctt Leu	gaa Glu	cgc Arg	: gga ; Gly 15	/ Gln	aag Lys	gct Ala	gcg Ala	Cac His 20	gcc Ala	163
ttt Phe	gca Ala	ctg Leu	ctg Leu 25	Met	att Ile	att	cag Gln	gga Gly 30	Ile	gct Ala	Pro	gtg Val	gta Val 35	Ala	ccg Pro	211
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tgg Trp	gca Ala 55	ctt Leu	gca Ala	ctg Leu	gtg Val	aat Asn 60	ttt Phe	gcg Ala	cag Gln	ctg Leu	ctt Leu 65	gtt Val	gct Ala	ttg Leu	ctg Leu	307
cag Gln 70	att Ile	aag Lys	gag Glu	tcg Ser	aag Lys 75	cca Pro	gtt Val	gaa Glu	gag Glu	cgt Arg 80	acc Thr	gca Ala	gca Ala	gga Gly	ctt Leu 85	355
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Leu	Ala	tat Tyr	Val	Phe	aca Thr	Leu	Gly	Leu	Ser	ttt Phe	ggg Gly	gcg Ala	atg Met 115	ttc Phe	tcc Ser	451
tac Tyr	att Ile	tcg Ser 120	gcg Ala	tcg Ser	ccg Pro	ttc Phe	gtg Val 125	ctg Leu	cag Gln	aat Asn	caa Gln	atg Met 130	ggc Gly	att Ile	ccg Pro	499
gta /al	ctg Leu 135	ctg Leu	tat Tyr	tcc Ser	att Ile	att Ile 140	ttc Phe	gga Gly	gtg Val	aat Asn	gct Ala 145	ttt Phe	ggt Gly	ttg Leu	att Ile	547
gtg	ggc	gga	atg	gtc	aat	agg	cga	ctt	ctg	cag	cgg	att	cat	cca	cac	595

Va: 150		y Gl	у Ме	t Va	1 As 15	n Ar	g Ar	g Lei	ı Leı	1 Gli 160	_	; Ile	His	Pro	His 165	
					r Va	g cto l Le				Thi						643
				u Va		g ttt u Phe			Trp					Leu		691
			e Lev			t tcc l Ser		Ile					Ala			739
		Lev				gtg Val 220	Val									787
	Ile					caa Gln					Ala					835
					/ Ser	gat Asp										883
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Lys	Ala	Ala	His 20	Ala	Phe	Ala	Leu	Leu 25	Met	Ile	Ile	Gln	Gly 30	Ile	Ala	
Pro	Val	Val 35	Ala	Pro	Leu	Ile	Gly 40	Gly	Val :	Leu	Val	Gly 45	Pro	Phe	Gly	
Trp	Arg 50	Gly	Ile	Phe	Trp	Ala : 55	Leu i	Ala 1	Leu '	Val	Asn 60	Phe	Ala	Gln	Leu	
Leu 65	Val	Ala	Leu	Leu	Gln 70	Ile	Lys (Glu S	Ser 1	Lys 75	Pro '	Val	Glu	Glu Z	Arg 80	

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85 90 95

Lys Asn Pro Gln Phe Leu Ala Tyr Val Phe Thr Leu Gly Leu Ser Phe 100 105 110

Gly Ala Met Phe Ser Tyr Ile Ser Ala Ser Pro Phe Val Leu Gln Asn 115 120 125

Gln Met Gly Ile Pro Val Leu Leu Tyr Ser Ile Ile Phe Gly Val Asn 130 135 140

Ala Phe Gly Leu Ile Val Gly Gly Met Val Asn Arg Arg Leu Leu Gln 145 150 155 160

Arg Ile His Pro His Arg Ile Met Gln Thr Val Leu Ala Ser Phe Thr 165 170 175

Val Leu Cys Ala Leu Leu Leu Ile Glu Val Leu Phe Ile Asn Trp Ile 180 185 190

Pro Leu Phe Leu Leu Leu Phe Leu Ile Val Ser His Ile Pro Met 195 200 205

Val Met Ala Asn Ala Thr Ala Leu Gly Thr Glu Val Val Arg Ser Arg 210 215 220

Ala Gly Ser Gly Ser Ala Ile Leu Gly Phe Val Gln Phe Thr Met Gly 225 235 240

Ala Leu Val Ser Ser Leu Val Gly Leu Gly Ser Asp Lys Ala Leu Thr 245 250 255

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Tyr Leu Ala Gly Arg Lys Gly Ile Pro Glu Met Lys 275 280

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	ctg Leu				Leu					ı Ala						163
tcc Ser	gcg Ala	cta Leu	gcg Ala 25	Thr	gat Asp	atg Met	tat Tyr	ttg Leu 30	Pro	gca Ala	atg Met	cct Pro	ggt Gly 35	att Ile	gcg Ala	211
	gat Asp		Gly					Met								259
	atg Met 55															307
	caa Gln										Gly					355
	gtc Val															403
	atc Ile															451
-	cgc Arg		-	_	-	-		-			_			_	_	499
_	cct Pro 135	-			tgai	gatt	at 1	tcag	ggaa	tt g	ct					537
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Met	Pro	Gly 35	Ile	Ala	Glu	Asp	Leu 40	Gly	Thr	Thr	Ala	Pro 45	Met	Val	Gln	
Leu	Thr 50	Leu	Ser	Ser	Phe	Met 55	Ala	Gly	Met	Ala	Ile 60	Gly	Gln	Leu	Ile	
Ile 65	Gly	Pro	Leu	Ser	Asp 70	Gln	Leu	Gly	Arg	Lys 75	Gly	Leu	Leu	Val	Ala 80	

Gly Ala Val Ala Ala Leu Val Ala Ser Val Val Cys Ala Leu Ala Pro Ser Ile Ser Val Leu Val Ile Ala Arg Leu Val Gln Gly Leu Gly Gly 105 Gly Ala Cys Val Val Leu Arg Ala Arg Ser Cys Gln Thr Leu Asn Ala 120 Asp Lys Arg Leu Arg Thr Pro Leu His Cys 130 <210> 131 <211> 501 <212> DNA <213> Corynebacterium glutamicum <220> <221> CDŞ <222> (101)..(478) <223> FRXA00901 <400> 131 acctgaatga aaatttctaa ttaaaaatac ccccaaatct tcgatataga tacacgagac 60 agtgatgcag aaaaaacaac agctgagcac cgccctgatt atg gga ttg gca tta 115 Met Gly Leu Ala Leu ttg tca gcc agc tcc gcg cta gcg act gat atg tat ttg ccg gca atg Leu Ser Ala Ser Ser Ala Leu Ala Thr Asp Met Tyr Leu Pro Ala Met 10 cct ggt att gcg gaa gat ttg ggg aca act gca ccg atg gtg cag tta 211 Pro Gly Ile Ala Glu Asp Leu Gly Thr Thr Ala Pro Met Val Gln Leu act ctt tct tcc ttt atg gct gga atg gcg att ggc caa ttg atc att Thr Leu Ser Ser Phe Met Ala Gly Met Ala Ile Gly Gln Leu Ile Ile 45 ggt cct ttg tcg gat caa ttg gga agg aaa ggc ctg ctc gtt gca ggt 307 Gly Pro Leu Ser Asp Gln Leu Gly Arg Lys Gly Leu Leu Val Ala Gly gcg gtg gct gcg ctg gtc gct agt gtg gtg tgc gcg ctg gcg ccg tcg 355 Ala Val Ala Ala Leu Val Ala Ser Val Val Cys Ala Leu Ala Pro Ser 75 ata age gta tta gtg ate gea ege etg gtg eag ggg ett gge gge ggt 403 Ile Ser Val Leu Val Ile Ala Arg Leu Val Gln Gly Leu Gly Gly Gly gcg tgc gtg gta ttg cgc gcg cga tcg tgc cag acc ttg aac gcg gac 451 Ala Cys Val Val Leu Arg Ala Arg Ser Cys Gln Thr Leu Asn Ala Asp

498

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120 125

gct 501

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<211> 126

<212> PRT

<213> Corynebacterium glutamicum

<400> 132

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Pro Met Val Gln Leu Thr Leu Ser Ser Phe Met Ala Gly Met Ala Ile 35 40 45

Gly Gln Leu Ile Ile Gly Pro Leu Ser Asp Gln Leu Gly Arg Lys Gly
50 55 60

Leu Leu Val Ala Gly Ala Val Ala Ala Leu Val Ala Ser Val Val Cys
65 70 75 80

Ala Leu Ala Pro Ser Ile Ser Val Leu Val Ile Ala Arg Leu Val Gln 85 90 95

Gly Leu Gly Gly Gly Ala Cys Val Val Leu Arg Ala Arg Ser Cys Gln 100 105 110

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Met Ser Thr Thr
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			Ala					Val					Ile		ctg Leu	259
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					gtg Val											931
			-		gtc Val		-	_				_		_		979
					cta Leu											1027
, ,			-	-	tac Tyr 315		_				_					1075
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PCT/IB00/00922

35 40 45

Ser Ser Ile Gly Leu Leu Met Thr Val Tyr Ala Thr Val Val Ala Val 50 60

Val Thr Ile Pro Ala Met Leu Trp Val Ser Arg Phe Asn Lys Arg Thr 65 70 75 80

Val Phe Leu Ile Thr Leu Ala Phe Leu Ala Thr Gly Ile Val Val Gln 85 90 95

Ala Leu Thr Val Asn Tyr Gly Met Leu Ala Ile Gly Arg Thr Ile Ala 100 105 110

Ala Leu Thr His Gly Val Phe Trp Ala Leu Val Gly Pro Met Ala Ala 115 120 125

Arg Met Ser Pro Gly His Thr Gly Arg Ala Val Gly Val Val Ser Ile 130 140

Gly Ser Thr Met Ala Leu Val Val Gly Ser Pro Leu Ala Thr Trp Ile 145 150 155 160

Gly Glu Leu Ile Gly Trp Arg Pro Ala Thr Trp Ile Leu Gly Ala Leu $165 \cdot 170$ 175

Thr Ile Ala Ala Val Ala Val Leu Ile Pro Thr Val Pro Ser Leu Pro 180 185 190

Pro Leu Pro Asp Thr Glu Ser Glu Ser Lys Glu Lys Lys Ser Leu Pro 195 200 205

Trp Gly Leu Ile Ser Leu Val Ile Phe Leu Leu Leu Ala Val Thr Gly 210 215 220

Val Phe Ala Ala Tyr Thr Tyr Leu Gly Leu Ile Ile Ala Glu Thr Ala 225 230 235 240

Gly Asp Ser Phe Val Ser Ile Gly Leu Phe Ala Phe Gly Ala Leu Gly 245 250 255

Leu Ile Gly Val Thr Val Ala Thr Arg Thr Val Asp Gln Arg Met Leu 260 265 270

Arg Gly Ser Val His Thr Thr Thr Leu Phe Val Ile Ala Ala Ile Leu 275 280 285

Gly Gln Ile Ala Phe Gly Leu Glu Gly Thr Leu Ala Val Val Ala Ile 290 295 300

Phe Leu Ala Val Thr Val Phe Gly Gly Ala Tyr Gly Ala Leu Pro Thr 305 310 315 320

Leu Gly Thr Thr Ile Phe Leu His Ala Gly Arg Asp His Pro Asp Thr 325 330 335

Ala Ser Ser Ile Tyr Val Val Thr Tyr Gln Val Gly Ile Ala Ser Gly

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420

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Gly Gly Phe Ala Ile Gly Val Thr Glu Phe Val Ser Met Gly Leu Leu 55 60 age geg ate gee tee gae ttt gag ate tee gaa gae caa gee gga cae 355 Ser Ala Ile Ala Ser Asp Phe Glu Ile Ser Glu Asp Gln Ala Gly His 70 75 80 379 atc atc acc atc tac gcc ctc gcg Ile Ile Thr Ile Tyr Ala Leu Ala 90 <210> 138 <211> 93 <212> PRT <213> Corynebacterium glutamicum <400> 138 Met His Glu Ser Gly Lys Asn Pro Val Lys Val Val Asp Ser Gln Ala Pro Gln Gly Arg Gly Gly His Ile Gly Gly His Ile Lys Arg Pro Ile Pro Arg Gln Thr Glu Ile Ser Glu Val Arg Arg Tyr Ile Val Met Thr Ala Leu Ala Leu Gly Gly Phe Ala Ile Gly Val Thr Glu Phe Val 55 Ser Met Gly Leu Leu Ser Ala Ile Ala Ser Asp Phe Glu Ile Ser Glu Asp Gln Ala Gly His Ile Ile Thr Ile Tyr Ala Leu Ala <210> 139 <211> 735 <212> DNA <213> Corynebacterium glutamicum <220> <221> CDS <222> (101)..(712) <223> RXA00109 aagtggggga agatttcgac aactaaccgg gcgcaaagat gaaactaatg cgtccgacca 60 cggcgaaaag gaagtttcgc ccatctatga gaggttgaat gtg gct tca gag aag Val Ala Ser Glu Lys 1 aat cta aaa ttg cgt acc ttg gcg gca gct gct ggg gtg ttg ggc gtt 163

20

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Asn Leu Lys Leu Arg Thr Leu Ala Ala Ala Gly Val Leu Gly Val

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		gat Asp 40	Ser					Gly					Glu			259
gag Glu	acc Thr 55	att	gag Glu	ttg Leu	gag Glu	ttt Phe 60	tcc Ser	ggt Gly	att	cct Pro	cag Gln 65	Asp	ctg Leu	ttc Phe	aca Thr	307
aca Thr 70	gtt Val	gca Ala	ttg Leu	agc Ser	aat Asn 75	gcg Ala	gat Asp	tcc Ser	gga Gly	gag Glu 80	Val	tta Leu	act Thr	tct Ser	gga Gly 85	355
act Thr	cct Pro	cag Gln	ctt Leu	gag Glu 90	ggg Gly	cag Gln	cac His	ttg Leu	agc Ser 95	tat Tyr	gaa Glu	gtg Val	cca Pro	tct Ser 100	gat Asp	403
gtg Val	cag Gln	acg Thr	gga Gly 105	gct Ala	ggt Gly	aac Asn	Tyr	att Ile 110	ttg Leu	ggt Gly	ttc Phe	cag Gln	atc Ile 115	act Thr	tct Ser	451
tct Ser	gat Asp	ggt Gly 120	cac His	gct Ala	act Thr	aaa Lys	ggt Gly 125	tca Ser	atc Ile	tct Ser	ttt Phe	gag Glu 130	gtg Val	aca Thr	ggc Gly	499
		gaa Glu														547
gca Ala 150	gca Ala	acc Thr	act Thr	gac Asp	acc Thr 155	tca Ser	gag Glu	acc Thr	acc Thr	gaa Glu 160	gca Ala	gag Glu	aca Thr	act Thr	gaa Glu 165	595
act Thr	gct Ala	gat Asp	gaa Glu	act Thr 170	tct Ser	gga Gly	att Ile	cct Pro	gcg Ala 175	ccg Pro	tgg Trp	aat Asn	tgg Trp	gtt Val 180	ttg Leu	643
		gtg Val														691
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<213> Corynebacterium glutamicum

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Ala	Ala	His 35	_	Val	Val	Val	Asp 40	Ser	Asn	Pro	Glu	Asn 45	_	Ser	Val	
Val	Asp 50		Phe	Pro	Glu	Thr 55	Ile	Glu	Leu	Glu	Phe 60		Gly	Ile	Pro	
Gln 65		Leu	Phe	Thr	Thr 70	Val	Ala	Leu	Ser	Asn 75	Ala	Asp	Ser	Gly	Glu 80	
Val	Leu	Thr	Ser	Gly 85	Thr	Pro	Gln	Leu	Glu 90	Gly	Gln	His	Leu	Ser 95	Tyr	
Glu	Val	Pro	Ser 100	Asp	Val	Gln	Thr	Gly 105	Ala	Gly	Asn	Tyr	Ile 110	Leu	Gly	
Phe	Gln	Ile 115	Thr	Ser	Ser	Asp	Gly 120	His	Ala	Thr	Lys	Gly 125	Ser	Ile	Ser	
Phe	Glu 130	Val	Thr	Gly	Ser	Ala 135	Glu	Thr	Thr	Thr	Glu 140	Thr	Thr	Ala	Glu	
Thr 145	Thr	Thr	Glu		Ala 150	Ala	Thr	Thr	Asp	Thr 155	Ser	Glu	Thr	Thr	Glu 160	
Ala	Glu	Thr	Thr	Glu 165	Thr	Ala	Asp	Glu	Thr 170	Ser	Gly	Ile	Pro	Ala 175	Pro	
Trp	Asn	Trp	Val 180	Leu	Ser	Ile		Ala 185	Val	Leu	Val	Val	Ala 190	Ser	Ala	
Ile	Val	Met 195	Met	Ile	Ala	Lys .	Asn 2 200	Arg .	Asn	Gln	Lys					
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cggc										at q	gtg (tca (gag	aag	115
aat d	cta a	aaa t	tg c	gt a	cc t	tg g	cg g	ca g	ct g	ct g	igg q	gtg t	tg (ggc (gtt	163

Giy Ala Met Ser Met Leu Val Ala Pro Gin Ala Ala Ala Ala His Asp Val 25 gtg gtg gat tct aat cct gaa aat ggc agt gtc gtt gat gag ttc ccg 2 Val Val Asp Ser Asn Pro Glu Asn Gly Ser Val Val Asp Glu Phe Pro 40 45 gag acc att gag ttg gag ttt tcc ggt att cct cag gat ctg ttc aca 3 Glu Thr Ile Glu Leu Glu Phe Ser Gly Ile Pro Gln Asp Leu Phe Thr 55 aca gtt gca ttg agc aat gcg gat tcc gga gag gtg tta act tct gga 3 Thr Val Ala Leu Ser Asn Ala Asp Ser Gly Glu Val Leu Thr Ser Gly 70 act cct cag ctt gag ggg cag cac ttg agc tat gaa gtg cca tct gat Thr Pro Gln Leu Glu Gly Gln His Leu Ser Tyr Glu Val Pro Ser Asp 90 gtg cag acg gga gct ggt aac tac att ttg ggt ttc cag atc act tct Val Gln Thr Gly Ala Gly Asn Tyr Ile Leu Gly Phe Gln Ile Thr Ser Ilo 105 tct gat ggt cac gct act aaa ggt tca atc tct ttt gag gtg aca ggc Ser Asp Gly His Ala Thr Lys Gly Ser Ile Ser Phe Glu Val Thr Gly 120 tct gct gaa acg aca aca gag aca aca gca gag acg ac	Asn	Leu	Lys	Leu	Arg	Thr	Leu	Ala	Ala	Ala 15	Ala	Gly	Val	Leu	Gly 20	Val	
Val Val Asp Ser Asn Pro Glu Asn Gly Ser Val Val Asp Glu Phe Pro 40 gag acc att gag ttg gag ttt tcc ggt att cct cag gat ctg ttc aca Glu Thr Ile Glu Leu Glu Phe Ser Gly Ile Pro Gln Asp Leu Phe Thr 55 aca gtt gca ttg agc aat gcg gat tcc gga gag gtg tta act tct gga Thr Val Ala Leu Ser Asn Ala Asp Ser Gly Glu Val Leu Thr Ser Gly 70 act cct cag ctt gag ggg cag cac ttg agc tat gaa gtg cca tct gat Thr Pro Gln Leu Glu Gly Gln His Leu Ser Tyr Glu Val Pro Ser Asp 90 gtg cag acg gga gct ggt aac tac att ttg ggt ttc cag atc act tct Val Gln Thr Gly Ala Gly Asn Tyr Ile Leu Gly Phe Gln Ile Thr Ser 110 tct gat ggt cac gct act aaa ggt tca atc tct ttt gag gtg aca ggc Ser Asp Gly His Ala Thr Lys Gly Ser Ile Ser Phe Glu Val Thr Gly 120 tct gct gaa acg aca aca aca gag aca aca gca gag aca act gag tca Ser Ala Glu Thr Thr Thr Thr Glu Thr 130 gca gca acc act gac acc tca gag acc acc gaa gca gac aca act gag Ala Ala Thr Thr Asp Thr Ser Glu Thr Thr Glu Ala Glu Thr Thr Glu 155 act gct gat gaa act tct gga att cct gcg ccg tgg aat tgg gtt ttg Thr Ala Asp Glu Thr Ser Gly Ile Pro Ala Pro Trp Asn Trp Val Leu 170 agc atc gtg gcg aca cag aca aca gaa taagaggtt tattcaccat gaa Ala Ala Thr Ala Asp Glu Thr Ser Gly Ile Pro Ala Pro Trp Asn Trp Val Leu 170 agc atc gtg gcg gtg Ser Ile Val Ala Val Leu Val Val Ala Ser Ala Ile Val Met Met Ile 185 gca aag aat cgt aac cag aaa taagagggtt tattcaccat gaa Ala Lys Asn Arg Asn Gln Lys			-	Ser	Met			_	Pro	-	-	-	-	His	_		21:
Glu Thr Ile Glu Leu Glu Phe Ser Gly Ile Pro Gln Asp Leu Phe Thr 60 aca gtt gca ttg agc aat gcg gat tcc gga gag gtg tta act tct gga Thr Val Ala Leu Ser Asn Ala Asp Ser Gly Glu Val Leu Thr Ser Gly 70 75 act cct cag ctt gag ggg cag cac ttg agc tat gaa gtg cca tct gat Thr Pro Gln Leu Glu Gly Gln His Leu Ser Tyr Glu Val Pro Ser Asp 90 gtg cag acg gga gct ggt aac tac att ttg ggt ttc cag atc act tct Val Gln Thr Gly Ala Gly Asn Tyr Ile Leu Gly Phe Gln Ile Thr Ser 105 tct gat ggt cac gct act aaa ggt tca atc tct ttt gag gtg aca ggc Ser Asp Gly His Ala Thr Lys Gly Ser Ile Ser Phe Glu Val Thr Gly 120 tct gct gaa acg aca aca gag aca aca aca gca gag aca act gag tca Ser Ala Glu Thr Thr Thr Glu Thr Thr Ala Glu Thr Thr Thr Glu Ser 135 gca gca acc act gac acc tca gag acc acc gag gca gag aca act gag Ser Ala Ala Thr Thr Asp Thr Ser Glu Thr Thr Glu Ala Glu Thr Thr Glu 155 act gct gat gaa act tct gga att cct gcg ccg tgg aat tgg gtt ttg Thr Ala Asp Glu Thr Ser Gly Ile Pro Ala Pro Trp Asn Trp Val Leu 170 agc atc gtg gcg gtg ctt gtt gtt gca agt gcc atc gtc atg atg Ala Ala Val Leu Val Val Ala Ser Ala Ile Val Met Met Ile 185 gca aag aat cgt aac cag aaa taagagggtt tattcaccat gaa 75 Ala Lys Asn Arg Asn Gln Lys			Asp	Ser			_	Asn		_	-	_	Asp				259
Thr Val Ala Leu Ser Asn Ala Asp Ser Gly Glu Val Leu Thr Ser Gly 85 act cct cag ctt gag ggg cag cac ttg agc tat gaa gtg cca tct gat Thr Pro Gln Leu Glu Gly Gln His Leu Ser Tyr Glu Val Pro Ser Asp 90 gtg cag acg gga gct ggt aac tac att ttg ggt ttc cag atc act tct 4 Val Gln Thr Gly Ala Gly Asn Tyr Ile Leu Gly Phe Gln Ile Thr Ser 110 tct gat ggt cac gct act aaa ggt tca atc tct ttt gag gtg aca gcg Ser Asp Gly His Ala Thr Lys Gly Ser Ile Ser Phe Glu Val Thr Gly 120 tct gct gaa acg aca aca aca gag aca aca gca gag acg ac		Thr			_		Phe					Gln	-	-			301
Thr Pro Gln Leu Glu Gly Gln His Leu Ser Tyr Glu Val Pro Ser Asp 90 95 100 gtg cag acg gga gct ggt aac tac att ttg ggt ttc cag atc act tct Val Gln Thr Gly Ala Gly Asn Tyr Ile Leu Gly Phe Gln Ile Thr Ser 110 115 tct gat ggt cac gct act aaa ggt tca atc tct ttt gag gtg aca ggc Aser Asp Gly His Ala Thr Lys Gly Ser Ile Ser Phe Glu Val Thr Gly 120 125 tct gct gaa acg aca aca gag aca aca gca gag acg ac	Thr					Asn					Glu					Gly	355
Val Gln Thr Gly Ala Gly Asn Tyr Ile Leu Gly Phe Gln Ile Thr Ser 105 tct gat ggt cac gct act aaa ggt tca atc tct ttt gag gtg aca ggc 4 Ser Asp Gly His Ala Thr Lys Gly Ser Ile Ser Phe Glu Val Thr Gly 125 tct gct gaa acg aca aca gag aca aca gca gag acg ac			_		Glu		_		-	Ser		_			Ser	•	403
Ser Asp Gly His Ala Thr Lys Gly Ser Ile Ser Phe Glu Val Thr Gly 120 tet get gaa acg aca aca gag aca aca gea gag acg acg aca act gag tea Ser Ala Glu Thr Thr Thr Glu Thr Thr Ala Glu Thr Thr Thr Glu Ser 135 gea gea acc act gac acc tea gag acc acc gaa gea gea gag aca act gaa 59 Ala Ala Thr Thr Asp Thr Ser Glu Thr Thr Glu Ala Glu Thr Thr Glu 165 act get gat gaa act tet gga att cet geg ceg tgg aat tgg gtt ttg 165 act get gat gaa act tet gga att cet geg ceg tgg aat tgg gtt ttg 170 Thr Ala Asp Glu Thr Ser Gly Ile Pro Ala Pro Trp Asn Trp Val Leu 170 age ate gtg geg gtg ett gtt gt gea agt gec ate gte atg atg atg 180 age ate gtg geg gtg ett gtt gt gea agt gec ate gte atg atg atg 180 Ser Ile Val Ala Val Leu Val Val Ala Ser Ala Ile Val Met Met Ile 190 gea aag aat egt aac cag aaa taagagggtt tatteaccat gaa Ala Lys Asn Arg Asn Gln Lys				Gly					Ile					Ile			451
Ser Ala Glu Thr Thr Thr Glu Thr Thr Ala Glu Thr Thr Thr Glu Ser 135 gca gca acc act gac acc tca gag acc acc gaa gca gag aca act gaa Ala Ala Thr Thr Asp Thr Ser Glu Thr Thr Glu Ala Glu Thr Thr Glu 150 act gct gat gaa act tct gga att cct gcg ccg tgg aat tgg gtt ttg Thr Ala Asp Glu Thr Ser Gly Ile Pro Ala Pro Trp Asn Trp Val Leu 170 agc atc gtg gcg gtg ctt gtt gtt gca agt gcc atc gtc atg atg att Ser Ile Val Ala Val Leu Val Val Ala Ser Ala Ile Val Met Met Ile 185 gca aag aat cgt aac cag aaa taagagggtt tattcaccat gaa Ala Lys Asn Arg Asn Gln Lys		-	Gly		-			Ğĺy					Glu				499
Ala Ala Thr Thr Asp Thr Ser Glu Thr Thr Glu Ala Glu Thr Thr Glu 150 act gct gat gaa act tct gga att cct gcg ccg tgg aat tgg gtt ttg Thr Ala Asp Glu Thr Ser Gly Ile Pro Ala Pro Trp Asn Trp Val Leu 170 agc atc gtg gcg gtg ctt gtt gtt gca agt gcc atc gtc atg atg att Ser Ile Val Ala Val Leu Val Val Ala Ser Ala Ile Val Met Met Ile 185 gca aag aat cgt aac cag aaa taagagggtt tattcaccat gaa Ala Lys Asn Arg Asn Gln Lys		Ala	-	_			Glu			-		Thr					547
Thr Ala Asp Glu Thr Ser Gly Ile Pro Ala Pro Trp Asn Trp Val Leu 170 agc atc gtg gcg gtg ctt gtt gtt gca agt gcc atc gtc atg atg att Ser Ile Val Ala Val Leu Val Val Ala Ser Ala Ile Val Met Met Ile 185 190 195 gca aag aat cgt aac cag aaa taagagggtt tattcaccat gaa Ala Lys Asn Arg Asn Gln Lys	Ala					Thr					Glu					Glu	595
Ser Ile Val Ala Val Leu Val Val Ala Ser Ala Ile Val Met Met Ile 185 190 195 gca aag aat cgt aac cag aaa taagagggtt tattcaccat gaa 73 Ala Lys Asn Arg Asn Gln Lys		-	-	-	Thr					Ála	_				Val	-	643
Ala Lys Asn Arg Asn Gln Lys				Ala					Ala					Met			691
			Asn					taag	aggg	tt t	atto	acca	it ga	a			735

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<213> Corynebacterium glutamicum

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Ala Ala His Asp Val Val Val Asp Ser Asn Pro Glu Asn Gly Ser Val 35 40 45

Val Asp Glu Phe Pro Glu Thr Ile Glu Leu Glu Phe Ser Gly Ile Pro 50 55 60

Gln Asp Leu Phe Thr Thr Val Ala Leu Ser Asn Ala Asp Ser Gly Glu 65 70 75 80

Val Leu Thr Ser Gly Thr Pro Gln Leu Glu Gly Gln His Leu Ser Tyr 85 90 95

Glu Val Pro Ser Asp Val Gln Thr Gly Ala Gly Asn Tyr Ile Leu Gly 100 105 110

Phe Gln Ile Thr Ser Ser Asp Gly His Ala Thr Lys Gly Ser Ile Ser 115 120 125

Phe Glu Val Thr Gly Ser Ala Glu Thr Thr Thr Glu Thr Thr Ala Glu 130 135 140

Thr Thr Thr Glu Ser Ala Ala Thr Thr Asp Thr Ser Glu Thr Thr Glu 145 150 155 160

Ala Glu Thr Thr Glu Thr Ala Asp Glu Thr Ser Gly Ile Pro Ala Pro 165 170 175

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<213> Corynebacterium glutamicum

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Met Ser Thr Val Thr

1 5

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				Lys					Asp		gat Asp			Val	gag Glu	211
			Ile					Gly			ggc					259
											ttc Phe 65					307
	Val		-	_		-		_	-		ctg Leu	-				355
		-				_	-	-			gat Asp	_	_			403
_			_				_	-	Āla		gga Gly					451
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											cgc Arg 145					547
		-				-			_		ttg Leu	-	-	-		595
				_	-						gca Ala	_		-		643
											gtt Val					691
	_		-	_			-	_			att Ile	_		_	_	739
											ctt Leu 225					787

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<213> Corynebacterium glutamicum

<400> 144

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35 40 45

Gly Ser Gly Lys Thr Thr Leu Met Arg Ala Ile Val Gly Val Gln Asn 50 60

Phe Asp Gly Thr Leu Glu Val Phe Asp Gln Pro Ala Gly Ala Ala Ser 65 70 75 80

Leu Arg Gly Lys Ile Gly Tyr Val Thr Gln Asn Ala Ser Val Tyr His $85 \hspace{1cm} 90 \hspace{1cm} 95$

Asp Leu Ser Val Ile Glu Asn Leu Lys Tyr Phe Gly Ala Leu Ala Lys 100 105 110

Gly Thr Ser Thr Pro Arg Thr Pro Glu Lys Ile Leu Glu Val Leu Asp 115 120 125

Ile Ala Asp Leu Ala Gln Arg Gln Val Ser Thr Leu Ser Gly Gln
130 135 140

Arg Gly Arg Val Ser Leu Gly Cys Ala Leu Ile Ala Ser Pro Glu Leu 145 150 155 160

Leu Val Met Asp Glu Pro Thr Val Gly Leu Asp Pro Ile Thr Arg Gln
165 170 175

Ala Leu Trp Glu Glu Phe Thr Thr Ile Ala Lys Ala Gly Ala Gly Val 180 185 190

Val Ile Ser Ser His Val Leu Glu Glu Ala Ala Arg Cys Asp Asn Leu 195 200 205

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tct acg gtg ggt acc gca act gat gcc acc gcg atg ttg cgc att ttg

Ser Thr Val Gly Thr Ala Thr Asp Ala Thr Ala Met Leu Arg Ile Leu

ttt tcc cga atc gcg gaa cct aac gcg ggt ggc ccg gga gct tat tcc

Phe Ser Arg Ile Ala Glu Pro Asn Ala Gly Gly Pro Gly Ala Tyr Ser

125

105

120

95

451

499

547

115

130

Phe Asn Val Pro Ser Val Ser Ala Ser Gly Ala Ile Thr Val Glu Lys 135 140 ggc gga aac acc aag cgg gag aaa gct acc ttc aaa cgc acg ggt ggc 595 Gly Gly Asn Thr Lys Arg Glu Lys Ala Thr Phe Lys Arg Thr Gly Gly 150 160 atg tgc cca gcg tgc gag ggc atg ggc agg gcc tca gac atc gac ctc 643 Met Cys Pro Ala Cys Glu Gly Met Gly Arg Ala Ser Asp Ile Asp Leu 170 aaa gag ctt ttc gac gcc tcc ctc tcc ctc aac gac ggc gcc ctg acc 691 Lys Glu Leu Phe Asp Ala Ser Leu Ser Leu Asn Asp Gly Ala Leu Thr atc ccc ggt tac acc cca ggt gga tgg agt tat cqq atq tat tca gaa 739 Ile Pro Gly Tyr Thr Pro Gly Gly Trp Ser Tyr Arg Met Tyr Ser Glu 200 205 tcg ggc ctt ttt gat gct gcc aag ccg att aag gat ttc acc gag gaa 787 Ser Gly Leu Phe Asp Ala Ala Lys Pro Ile Lys Asp Phe Thr Glu Glu 215 220 gaa cgc cac aac ttc ctt tat ctt gag ccc acc aag atg aag atc gct 835 Glu Arg His Asn Phe Leu Tyr Leu Glu Pro Thr Lys Met Lys Ile Ala 235 ggc atc aac atg acc tat gag ggt ctt atc ccc cgc att cag aaa tcc 883 Gly Ile Asn Met Thr Tyr Glu Gly Leu Ile Pro Arg Ile Gln Lys Ser 250 255 260 atg ttg tct aag gat cgc gaa ggc atg cag aag cat att cgt gcg ttc 931 Met Leu Ser Lys Asp Arg Glu Gly Met Gln Lys His Ile Arg Ala Phe 270 gtg gat cga gcg gtt acc ttc att cct tgc cct gcg tgt gga act Val Asp Arg Ala Val Thr Phe Ile Pro Cys Pro Ala Cys Gly Gly Thr 285 cga tta gcg cca cat gcc ttg gag tcc aag atc aat ggc aaa aac atc 1027 Arg Leu Ala Pro His Ala Leu Glu Ser Lys Ile Asn Gly Lys Asn Ile 300 gct gag ttg tgc gcg atg gag gtc cgt gat ttg gcc aag tgg atc aaa 1075 Ala Glu Leu Cys Ala Met Glu Val Arg Asp Leu Ala Lys Trp Ile Lys 310 315 acg gtg gaa gcc ccc tcg gtt gct ccc ctq ctc acc qca ctq act qaa 1123 Thr Val Glu Ala Pro Ser Val Ala Pro Leu Leu Thr Ala Leu Thr Glu 330 acc ctg gat aac ttc gtg gag atc ggt ttg ggc tat atc caa ctc gat 1171 Thr Leu Asp Asn Phe Val Glu Ile Gly Leu Gly Tyr Ile Gln Leu Asp 350 cgc ccc gct ggc acg ttg tct ggt ggt gag gca cag cgc acc aag atg 1219 Arg Pro Ala Gly Thr Leu Ser Gly Gly Glu Ala Gln Arg Thr Lys Met

360 365 370

		, His					Lei					Tyr			gat Asp	1267
	Pro					His					e Glu				aag Lys 405	1315
ttg Leu	ctg Leu	Leu	gat Asp	ctt Leu 410	ı Arg	gat Asp	aaa Lys	ggc Gly	aat Asn 415	Thr	gtt Val	tta Leu	gtc Val	yatç Val 420	gag Glu	1363
				Thr					Asp					Leu	ggg	1411
			Gly					Glu					Gly		gtc Val	1459
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atc Ile	cgc Arg	Gly	gcc Ala	gat Asp 490	cga Arg	aat Asn	aat Asn	ttg Leu	aac Asn 495	aat Asn	gtg Val	gat Asp	gtc Val	gat Asp 500	att Ile	1603
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												gtt Val 530				1699
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			ttg Leu													2179
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			gat Asp													2275
atc Ile	gtc Val	atc Ile	gaa Glu	cac His 730	cac His	ctc Leu	ggc Gly	gtg Val	ctc Leu 735	gct Ala	cac His	gct Ala	gac Asp	cac His 740	atc Ile	2323
			ggc Gly 745													2371
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Asn Gly Lys Asn Ile Ala Glu Leu Cys Ala Met Glu Val Arg Asp Leu

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615 620 Ala Asp Val Leu Gly Leu Ser Ala Ala Asn Ala Tyr Glu Phe Phe Ala 630 635 Ala Lys Asp Ser Lys Ile Leu Pro Ala Ala Lys Ile Ala Lys Arg Leu 650 Val Asp Val Gly Leu Gly Tyr Ile Thr Leu Gly Gln Pro Leu Thr Thr 660 Leu Ser Gly Gly Glu Arg Gln Arg Leu Lys Leu Ala Thr His Met Ala Asp Lys Ala Thr Thr Phe Ile Leu Asp Glu Pro Thr Thr Gly Leu His Leu Ala Asp Val Lys Thr Leu Leu Asp Leu Phe Asp Gln Leu Val Asp 715 Asp Gly Lys Ser Val Ile Val Ile Glu His His Leu Gly Val Leu Ala His Ala Asp His Ile Ile Asp Val Gly Pro Gly Ala Gly Ser Asp Gly 745 Gly Ser Ile Val Phe Glu Gly Ser Pro Ala Glu Leu Ile Lys Thr Asp 755 760 Thr Pro Thr Gly Arg His Leu Lys Ala Tyr Val Asp 775 <210> 147 <211> 278 <212> DNA <213> Corynebacterium glutamicum <220> <221> CDS <222> (1)..(255) <223> FRXA00829 <400> 147 ttg gat gag eec acc aca gge etg eac etc get gat gtg aaa acc ttg Leu Asp Glu Pro Thr Thr Gly Leu His Leu Ala Asp Val Lys Thr Leu 1 5 ctg gat ctt ttt gat caa ctg gtt gat gac ggc aag tct gtc atc gtc 96 Leu Asp Leu Phe Asp Gln Leu Val Asp Asp Gly Lys Ser Val Ile Val 20 25 atc gaa cac cac ctc ggc gtg ctc gct cac gct gac cac atc att gat Ile Glu His His Leu Gly Val Leu Ala His Ala Asp His Ile Ile Asp 35 40 45

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Val Gly Pro Gly Ala Gly Ser Asp Gly Gly Ser Ile Val Phe Glu Gly 50 55 age eee geg gaa etc atc aaa aet gat act eea aca gga ege eac ett 240 Ser Pro Ala Glu Leu Ile Lys Thr Asp Thr Pro Thr Gly Arg His Leu 65 70 75 aaa gct tat gta gat tagtttctta tggaaaaccc tgg 278 Lys Ala Tyr Val Asp <210> 148 <211> 85 <212> PRT <213> Corynebacterium glutamicum Leu Asp Glu Pro Thr Thr Gly Leu His Leu Ala Asp Val Lys Thr Leu Leu Asp Leu Phe Asp Gln Leu Val Asp Asp Gly Lys Ser Val Ile Val Ile Glu His His Leu Gly Val Leu Ala His Ala Asp His Ile Ile Asp Val Gly Pro Gly Ala Gly Ser Asp Gly Gly Ser Ile Val Phe Glu Gly Ser Pro Ala Glu Leu Ile Lys Thr Asp Thr Pro Thr Gly Arg His Leu Lys Ala Tyr Val Asp <210> 149 <211> 1663 <212> DNA <213> Corynebacterium glutamicum <220> <221> CDS <222> (101)..(1663) <223> FRXA00834 <400> 149 tgttttagcc atggacccca tactagggag agttttgttt tggtgctaga aaaggttcac 60 caagegegaa caggeetatg caaaeggtae gatatgacae atg caa aaa get gat Met Gln Lys Ala Asp 1 tcc cat gat tgg att tcg gtc cac ggt gcg aat gaa aac aac ctc aaa 163 Ser His Asp Trp Ile Ser Val His Gly Ala Asn Glu Asn Asn Leu Lys 10 20

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- ccg ctc ggc gtg ttc acg gcg att tcc ggc gtt gca ggt tcg ggt aag 1651
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Gly Thr Ile Ala Ala Glu Ser Arg Arg Leu Ile Asn Glu Thr Tyr Ser 50 60

Thr Phe Val Gln Gly Phe Met Pro Ser Met Ala Arg Pro Asp Val Asp 65 70 75 80

His Leu Glu Gly Ile Thr Thr Ala Ile Ile Val Asp Gln Glu Gln Met 85 90 95

Gly Ala Asn Pro Arg Ser Thr Val Gly Thr Ala Thr Asp Ala Thr Ala 100 105 110

Met Leu Arg Ile Leu Phe Ser Arg Ile Ala Glu Pro Asn Ala Gly Gly 115 120 125

Pro Gly Ala Tyr Ser Phe Asn Val Pro Ser Val Ser Ala Ser Gly Ala 130 135 140

Ile Thr Val Glu Lys Gly Gly Asn Thr Lys Arg Glu Lys Ala Thr Phe 145 150 155 160

Lys Arg Thr Gly Gly Met Cys Pro Ala Cys Glu Gly Met Gly Arg Ala 165 170 175

Ser Asp Ile Asp Leu Lys Glu Leu Phe Asp Ala Ser Leu Ser Leu Asn 180 185 190

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- Asp Phe Thr Glu Glu Glu Arg His Asn Phe Leu Tyr Leu Glu Pro Thr 225 230 235 240
- Lys Met Lys Ile Ala Gly Ile Asn Met Thr Tyr Glu Gly Leu Ile Pro 245 250 255
- Arg Ile Gln Lys Ser Met Leu Ser Lys Asp Arg Glu Gly Met Gln Lys 260 265 270
- His Ile Arg Ala Phe Val Asp Arg Ala Val Thr Phe Ile Pro Cys Pro 275 280 285
- Ala Cys Gly Gly Thr Arg Leu Ala Pro His Ala Leu Glu Ser Lys Ile 290 295 300
- Asn Gly Lys Asn Ile Ala Glu Leu Cys Ala Met Glu Val Arg Asp Leu 305 310 315 320
- Ala Lys Trp Ile Lys Thr Val Glu Ala Pro Ser Val Ala Pro Leu Leu 325 330 335
- Thr Ala Leu Thr Glu Thr Leu Asp Asn Phe Val Glu Ile Gly Leu Gly 340 345 350
- Tyr Ile Gln Leu Asp Arg Pro Ala Gly Thr Leu Ser Gly Gly Glu Ala 355 360 365
- Gln Arg Thr Lys Met Ile Arg His Leu Gly Ser Ala Leu Thr Asp Val 370 375 380
- Thr Tyr Val Phe Asp Glu Pro Thr Ala Gly Leu His Ala Tyr Asp Ile 385 390 395 400
- Glu Arg Met Asn Lys Leu Leu Leu Asp Leu Arg Asp Lys Gly Asn Thr 405 410 415
- Val Leu Val Glu His Lys Pro Glu Thr Ile Ala Ile Ala Asp His
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- Val Val Asp Leu Gly Pro Gly Ala Gly Ala Gly Gly Glu Ile Arg
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 440
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- Phe Glu Gly Ser Val Asp Lys Leu Lys Asp Ser Asp Thr Val Thr Gly 450 455
- Leu His Phe Asn Asp Arg Ala Ser Leu Lys Glu Ser Val Arg Ala Pro 465 470 480
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								gat Asp 190								691
								gat Asp								739
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Leu	Met :	Leu	Met	Phe	Leu	Met	Thr	Ser	Val	Thr	Met	Gln	Arg	Glu	Arg	

Asn Ala Gly Thr Leu Glu Arg Leu Trp Thr Thr Asn Ile His Arg Val

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Thr	Glu 130	Ser	Glu	Trp	Trp	11e		Thr	Leu	Ile	Ala 140		Ile	Thr	Gly	
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Glu	Phe	Gln	Ala	Ile 165		Thr	Leu	Pro	Leu 170	Leu	Ile	Leu	Pro	Gln 175	Phe	
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Arg	Trp	Val 195	Ser	Asn	Val	Leu	Pro 200	Leu	Ser	Tyr	Ala	Val 205	Asp	Ala	Ala	
Leu	Glu 210	Ala	Ser	Arg	Thr	Gly 215	Ile	Gly	Gln	Gln	Val 220	Val	Val	Asn	Ile	
Ala 225	Ile	Суѕ	Ala	Ala	Phe 230	Ala	Val	Ser	Phe	Leu 235	Leu	Val	Ala	Ala	Leu 240	
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265 270 275

tct gga ttt ggt atc caa caa ttc ggt cct caa atc atg ggc acc tct Ser Gly Phe Gly Ile Gln Gln Phe Gly Pro Gln Ile Met Gly Thr Ser 285 aaa act cgc ggg ccg att ttg gcc atg ttc gtc aca gtc atc ggc atg 1027 Lys Thr Arg Gly Pro Ile Leu Ala Met Phe Val Thr Val Ile Gly Met 300 atc ggc gcg gtg atc gtg gtg atg aac cct cat cca tgg tgg gcg cta 1075 Ile Gly Ala Val Ile Val Val Met Asn Pro His Pro Trp Trp Ala Leu 315 320 gtt ggc tgc atg gcc ctc ggc ctg tct tat ggc ctg tgt atg ttc atg 1123 Val Gly Cys Met Ala Leu Gly Leu Ser Tyr Gly Leu Cys Met Phe Met ggg ttg gcg gaa act caa aac att gct cca cct att gat atg gca ggc 1171 Gly Leu Ala Glu Thr Gln Asn Ile Ala Pro Pro Ile Asp Met Ala Gly 345 350 ctg acg ggt att ttc tac tgc ctg acg tac gta ggt atg gtc ttt cca 1219 Leu Thr Gly Ile Phe Tyr Cys Leu Thr Tyr Val Gly Met Val Phe Pro 360 365 gcc ttg atg acc tgg ttg aat caa tgg ctc agt tac ccg ttc atg ctg 1267 Ala Leu Met Thr Trp Leu Asn Gln Trp Leu Ser Tyr Pro Phe Met Leu ggc ttt ggt gcg gtg atg gca act att tqt ctq atc att gtq agt ttt 1315 Gly Phe Gly Ala Val Met Ala Thr Ile Cys Leu Ile Ile Val Ser Phe 395 agt gca cgc cga ttc tgagaaacaa ctaaagtgag cca 1353 Ser Ala Arg Arg Phe

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35 40 45

Glu Gly Phe Phe Ser Asn Leu Phe Ile Asp Leu Leu Leu Val Phe Tyr 50 55 60

Ala Ile Gly Val Ala Val Gly Leu Leu Ala Ala Gly Pro Leu Ser Asp 65 70 75 80

- Arg Tyr Gly Arg Arg Ala Val Met Leu Pro Ala Pro Leu Ile Ala Ile 85 90 95
- Leu Gly Ser Ala Leu Ile Ala Ser Gly Glu Glu Thr Ala Ile Leu Ile 100 105 110
- Ala Ile Gly Arg Val Leu Ser Gly Ile Ser Val Gly Met Val Met Thr 115 120 125
- Ala Gly Gly Ser Trp Ile Lys Glu Leu Ser Ser Ser Arg Phe Glu Pro 130 135 140
- Gly Val Lys Thr Ser Ala Gly Ala Lys Arg Ala Ser Met Ser Leu Thr 145 150 155 160
- Gly Gly Phe Ala Leu Gly Pro Ala Leu Ala Gly Val Met Ala Gln Trp 165 170 175
- Leu Pro Leu Pro Gly Gln Leu Ala Tyr Val Leu His Ile Ile Leu Thr 180 185 190
- Leu Ile Leu Phe Pro Leu Leu Ile Thr Ala Pro Glu Thr Arg Gln Ser 195 200 205
- Ala His Leu Lys Thr Lys Gly Ser Phe Trp Ser Asp Val Leu Val Pro 210 · 220
- Ser Ala Leu Asp Lys Arg Phe Leu Phe Val Val Ala Pro Ile Gly Pro 225 230 235 240
- Trp Val Phe Gly Ala Ala Phe Thr Ala Tyr Ala Val Leu Pro Ser Gln 245 250 255
- Leu Arg Asp Met Val Ser Ala Pro Val Ala Tyr Ser Ala Leu Ile Ala 260 .265 270
- Leu Val Thr Leu Gly Ser Gly Phe Gly Ile Gln Gln Phe Gly Pro Gln 275 280 285
- Ile Met Gly Thr Ser Lys Thr Arg Gly Pro Ile Leu Ala Met Phe Val 290 295 300
- Thr Val Ile Gly Met Ile Gly Ala Val Ile Val Val Met Asn Pro His 305 310 315 320
- Pro Trp Trp Ala Leu Val Gly Cys Met Ala Leu Gly Leu Ser Tyr Gly 325 330 335
- Leu Cys Met Phe Met Gly Leu Ala Glu Thr Gln Asn Ile Ala Pro Pro 340 345 350
- Ile Asp Met Ala Gly Leu Thr Gly Ile Phe Tyr Cys Leu Thr Tyr Val 355 360 365

Gly Met Val Phe Pro Ala Leu Met Thr Trp Leu Asn Gln Trp Leu Ser

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gct ggt gca aaa Ala Gly Ala Lys 150	cgc gca tcg Arg Ala Ser 155	atg tct ttg Met Ser Leu	acc ggt ggt Thr Gly Gly 160	ttt gcg ctc y Phe Ala Leu 165	595
ggc cca gcg ctt Gly Pro Ala Leu	gct ggt gtg Ala Gly Val 170	atg gca cag Met Ala Gln 175	tgg ctg cca Trp Leu Pro	a caa cct gga o Gln Pro Gly 180	643
cag ttg gca tat Gln Leu Ala Tyr 185	gtt ttg cac Val Leu His	att att ctc Ile Ile Leu 190	act ctg att Thr Leu Ile	ttg ttc ccg Leu Phe Pro 195	691
ttg ctt att aca Leu Leu Ile Thr 200	·				703
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1 Ala Gln Arg Lys 20 Ala Trp Gly Gly	5 Val Trp Leu Asn Glu Phe	Ala Val Ala 25 Thr Pro Leu 40	Leu Ser Val Leu Val Phe	15 I Phe Thr Val 30 E Tyr Arg Gly	
Ala Gln Arg Lys 20 Ala Trp Gly Gly 35 Glu Gly Phe Phe	5 Val Trp Leu Asn Glu Phe Ser Asn Leu 55	Ala Val Ala 25 Thr Pro Leu 40 Phe Ile Asp	Leu Ser Val Leu Val Phe 45 Leu Leu Leu 60	15 Phe Thr Val 30 Tyr Arg Gly Val Phe Tyr	
Ala Gln Arg Lys 20 Ala Trp Gly Gly 35 Glu Gly Phe Phe 50 Ala Ile Gly Val	5 Val Trp Leu Asn Glu Phe Ser Asn Leu 55 Ala Val Gly 70	Ala Val Ala 25 Thr Pro Leu 40 Phe Ile Asp Leu Leu Ala	Leu Ser Val Leu Val Phe 45 Leu Leu Leu 60 Ala Gly Pro 75	15 Phe Thr Val 30 Tyr Arg Gly Val Phe Tyr Leu Ser Asp 80	
Ala Gln Arg Lys 20 Ala Trp Gly Gly 35 Glu Gly Phe Phe 50 Ala Ile Gly Val 65	Val Trp Leu Asn Glu Phe Ser Asn Leu 55 Ala Val Gly 70 Arg Ala Val 85	Ala Val Ala 25 Thr Pro Leu 40 Phe Ile Asp Leu Leu Ala Met Leu Pro 90	Leu Ser Val Leu Val Phe 45 Leu Leu Leu 60 Ala Gly Pro 75 Ala Pro Leu	15 Phe Thr Val 30 Tyr Arg Gly Val Phe Tyr Leu Ser Asp 80 Ile Ala Ile 95	
Ala Gln Arg Lys 20 Ala Trp Gly Gly 35 Glu Gly Phe Phe 50 Ala Ile Gly Val 65 Arg Tyr Gly Arg Leu Gly Ser Ala	Val Trp Leu Asn Glu Phe Ser Asn Leu 55 Ala Val Gly 70 Arg Ala Val 85 Leu Ile Ala	Ala Val Ala 25 Thr Pro Leu 40 Phe Ile Asp Leu Leu Ala Met Leu Pro 90 Ser Gly Glu 105	Leu Ser Val Leu Val Phe 45 Leu Leu Leu 60 Ala Gly Pro 75 Ala Pro Leu Glu Thr Ala	15 Phe Thr Val 30 Tyr Arg Gly Val Phe Tyr Leu Ser Asp 80 Ile Ala Ile 95 Ile Leu Ile 110 Val Met Thr	

Gly Val Lys Thr Ser Ala Gly Ala Lys Arg Ala Ser Met Ser Leu Thr

145 150 155 Gly Gly Phe Ala Leu Gly Pro Ala Leu Ala Gly Val Met Ala Gln Trp 165 Leu Pro Gln Pro Gly Gln Leu Ala Tyr Val Leu His Ile Ile Leu Thr 185 Leu Ile Leu Phe Pro Leu Leu Ile Thr <210> 157 <211> 1014 <212> DNA <213> Corynebacterium glutamicum <220> <221> CDS <222> (101)..(991) <223> RXA01407 <400> 157 atccggggaa cggatcccaa agatctcctt gatgccatcg cgtttttaac ctggccagct 60 ctggttgccc cagtgatcgc cccacttctg ggaggtcttc ttg caa gat acc att Leu Gln Asp Thr Ile ggt tgc cga tgg atc ttc ctc ctc aac gtg ccc tta gga atc atc gcg 163 Gly Cys Arg Trp Ile Phe Leu Leu Asn Val Pro Leu Gly Ile Ile Ala atc atg gct gga cta ttc atc cag ccc aag aac acg gcc gtg aat gtg 211 Ile Met Ala Gly Leu Phe Ile Gln Pro Lys Asn Thr Ala Val Asn Val aag cga ttt gat cgg cca ggt ttc ctc ggc gca atg ctg gtg atg gtg 259 Lys Arg Phe Asp Arg Pro Gly Phe Leu Gly Ala Met Leu Val Met Val 45 gcg caa gcc gtg att gcg gag tta att tgc agc aga agt ccg gcc gca 307 Ala Gln Ala Val Ile Ala Glu Leu Ile Cys Ser Arg Ser Pro Ala Ala ctt act atc tgt gca tgc ctc gtc tta agt gct gcg gtg gta tgc ggt 355 Leu Thr Ile Cys Ala Cys Leu Val Leu Ser Ala Ala Val Val Cys Gly ttt gta gtg cgc tgg ctg cga gtt cca ggc cga ctt ttt gat ctc agc 403 Phe Val Val Arg Trp Leu Arg Val Pro Gly Arg Leu Phe Asp Leu Ser 95 atc atg cgc atc cca ggt ttc cga gtg ggt aat tcc tcc qqa aqt atc 451 Ile Met Arg Ile Pro Gly Phe Arg Val Gly Asn Ser Ser Gly Ser Ile 110

			Val								ttc Phe					499
							-				ggt Gly 145	_	-		_	547
											ttc Phe					595
		_						-	_	-	ttt Phe			_	-	643
											cgt Arg					691
_	_				-	-			-	-	ggc Gly	_				739
			_	_				-	-		gtc Val 225	-				787
											acc Thr					8.35
											gcc Ala					883
		-			-			_	-	-	gcg Ala	_				931
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Thr Ala Val Asn Val Lys Arg Phe Asp Arg Pro Gly Phe Leu Gly Ala 35 40 45

Met Leu Val Met Val Ala Gln Ala Val Ile Ala Glu Leu Ile Cys Ser 50 60

Arg Ser Pro Ala Ala Leu Thr Ile Cys Ala Cys Leu Val Leu Ser Ala 65 70 75 80

Ala Val Val Cys Gly Phe Val Val Arg Trp Leu Arg Val Pro Gly Arg 85 90 95

Leu Phe Asp Leu Ser Ile Met Arg Ile Pro Gly Phe Arg Val Gly Asn 100 105 110

Ser Ser Gly Ser Ile Tyr Arg Leu Val Ile Thr Ala Ala Pro Phe Met 115 120 125

Phe Thr Leu Leu Phe Gln Val Ala Phe Gly Trp Ser Ala Thr Leu Ala 130 $$135\$

Gly Ala Met Val Val Ala Leu Phe Ala Gly Asn Val Ala Ile Lys Pro 145 150 155 160

Phe Thr Thr Pro Ile Ile Lys Arg Trp Asn Phe Lys Pro Val Leu Val 165 170 175

Phe Ser Asn Ala Ala Gly Ala Leu Val Leu Ala Thr Phe Leu Phe Val
180 185 190

Arg Ala Asp Thr Pro Leu Val Leu Ile Val Leu Leu Leu Phe Val Ser 195 200 205

Gly Ala Leu Arg Ser Leu Gly Phe Ser Ala Tyr Asn Thr Leu Gln Phe 210 215 220

Val Asp Ile Ser Pro Glu Gln Thr Ser Asn Ala Asn Val Leu Ser Ala 225 230 235 240

Thr Leu His Gln Leu Gly Met Ser Leu Gly Ile Ala Val Ala Val Ile 245 250 255

Ala Met Ser Leu Ala Pro Thr Ala Asn Trp Ala Phe Pro Leu Ala Ala 260 . 265 270

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	Met Arg Asn Asp Arg													
1 5														
tcc ttt agc gtt ccc att gcg cta ctt gcc gcg	gga gca ctg ttt cta 163													
Ser Phe Ser Val Pro Ile Ala Leu Leu Ala Ala 10 15	-													
10 15	20													
gaa atc ctc gac ggc acc atc ctg aca acc gca	gtg cca gct att gct 211													
Glu Ile Leu Asp Gly Thr Ile Leu Thr Thr Ala														
25 30	35													
cgt gac ttc ggt att gac gcc gtg gat gtc agc Arg Asp Phe Gly Ile Asp Ala Val Asp Val Ser														
40 45	50													
	30													
tac ttg gca gcc gca gca gct ggc att ccg ctg	cag ggt ggc 301													
Tyr Leu Ala Ala Ala Ala Gly Ile Pro Leu	Gln Gly Gly													
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Val Pro Ala Ile Ala Arg Asp Phe Gly Ile Asp	Ala Val Asp Val Ser													
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Ile Ala Leu Val Ala Tyr Leu Ala Ala Ala Ala	Ala Gly Ile Pro Leu													
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Cln Cly Cly														
Gln Gly Gly 65														

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tgg Trp	gca Ala	gcc	aat Asn 25	His	tto Phe	gcg Ala	tca Ser	gtg Val 30	Leu	gtg Val	ttg Leu	ato	cgt Arg 35	Glu	caa Gln	211
tta Leu	gac Asp	gta Val 40	Ser	ago	gtg Val	ctg Leu	gtc Val 45	Asn	ggc Gly	gct Ala	ttt Phe	ggt Gly 50	Ile	tat Tyr	gca Ala	259
ctg Leu	gga Gly 55	ctt Leu	ctt Leu	cca Pro	agt Ser	ttg Leu 60	ctc Leu	gca Ala	ggc Gly	ggt Gly	gtg Val 65	ctt Leu	gcc Ala	gac Asp	cgt Arg	307
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gga Gly	aac Asn	ctt Leu	tct Ser	ctt Leu 90	tta Leu	gcg Ala	ttt Phe	cat His	gat Asp 95	ggt Gly	cct Pro	tcc Ser	ctc Leu	ctg Leu 100	gta Val	403
gga Gly	cga Arg	ttc Phe	atc Ile 105	gtt Val	Gly	Leu	Gly	gtt Val 110	Gly	Leu	Val	Val	agc Ser 115	gcg Ala	ggc Gly	451
acc Thr	gca Ala	tgg Trp 120	gcg Ala	ggc Gly	aga Arg	ttg Leu	cgc Arg 125	gga Gly	gca Ala	agc Ser	ggc Gly	gtg Val 130	aca Thr	ttg Leu	gcc Ala	499
ggc Gly	att Ile 135	att Ile	ctg Leu	acc Thr	gcc Ala	ggt Gly 140	ttc Phe	atg Met	atg Met	ggg Gly	ccg Pro 145	att Ile	gtg Val	aca Thr	agt Ser	547
999 31y 150	ttg Leu	ggg Gly	atg Met	gcg Ala	tcg Ser 155	aca Thr	agc Ser	att Ile	att Ile	acg Thr 160	ccc Pro	ttt Phe	gcc Ala	ata Ile	agc Ser 165	595

gtt Val	gco Ala	cte Le	c teg u Sei	g cto Lei 170	ı Ile	gcç Ala	gtç Val	g gtt . Val	gto Val	Gly	ttt Phe	gcg Ala	ctt Leu	ggc Gly 180	Asp	643
gco Ala	cgc Arg	ago Sei	c acc Thr 185	Pro	g ago Ser	gca Ala	ctt Leu	ggc Gly 190	/ Ala	tco Ser	ago Ser	gga Gly	ato Ile 195	Lys	cac His	691
ga <i>a</i> Glu	cga Arg	ago Ser 200	. Met	aaa Lys	aag Lys	gcc Ala	ctc Leu 205	Ala	gtg Val	tcc Ser	ttg Leu	ccg Pro 210	Met	gca Ala	att Ile	739
tgg Trp	gtg Val 215	Ph€	ago Ser	tgc Cys	: atc	acc Thr 220	acc Thr	tcc Ser	ctg Leu	ato	gtg Val 225	atg Met	tcc Ser	gcg Ala	cgc Arg	787
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ttc Phe	gcg Ala	tgg Trp	ggt Gly 265	cgt Arg	ggc Gly	tcc Ser	gga Gly	atc Ile 270	gtg Val	ggc Gly	gcg Ala	ctg Leu	tgt Cys 275	gcc Ala	ctc Leu	931
gcg Ala	ggt Gly	ttt Phe 280	Ala	ctg Leu	gca Ala	gct Ala	ttt Phe 285	ggt Gly	ggc Gly	gac Asp	tcc Ser	att Ile 290	cca Pro	gtg Val	tgg Trp	979
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ctg Leu 310	cgc Arg	gaa Glu	ggc Gly	ctc Leu	ctc Leu 315	agc Ser	atc Ile	gaa Glu	act Thr	tac Tyr 320	acg Thr	cca Pro	ctc Leu	aac Asn	cga Arg 325	1075
cgt Arg	ggc Gly	acc Thr	ggc Gly	atc Ile 330	Gly	atc Ile	Tyr	Tyr	Val	ttc Phe	acg Thr	Tyr	Leu	gga Gly 340	Phe	1123
ggg Gly	ctg Leu	cca Pro	gtg Val 345	ctt Leu	ctc Leu	gac Asp	gcc Ala	ctc Leu 350	ctc Leu	ccg Pro	cac His	ctt Leu	ggc Gly 355	gcc Ala	tcc Ser	1171
att Ile	ccg Pro	ctg Leu 360	tac Tyr	gcg Ala	ctg Leu	Ala	gcg Ala 365	ctc Leu	gcc Ala	ctt Leu	ggc Gly	tcc Ser 370	gca Ala	gta Val	atc Ile	1219
cgc Arg	ggc Gly 375	gta Val	caa Gln	atc Ile	Lys	cgc Arg (380	ggg Gly	tat Tyr	gtg Val	gtt Val	taga	tttc	ta c	ctac	gacct	1272
gaa																1275

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<211> 384

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Leu Ile Arg Glu Gln Leu Asp Val Ser Ser Val Leu Val Asn Gly Ala 35 40 45

Phe Gly Ile Tyr Ala Leu Gly Leu Leu Pro Ser Leu Leu Ala Gly Gly 50 60

Val Leu Ala Asp Arg Phe Gly Ala Arg Met Val Val Leu Thr Gly Gly 65 70 75 80

Val Leu Ser Ala Leu Gly Asn Leu Ser Leu Leu Ala Phe His Asp Gly 85 90 95

Pro Ser Leu Leu Val Gly Arg Phe Ile Val Gly Leu Gly Val Gly Leu 100 105 110

Val Val Ser Ala Gly Thr Ala Trp Ala Gly Arg Leu Arg Gly Ala Ser 115 120 125

Gly Val Thr Leu Ala Gly Ile Ile Leu Thr Ala Gly Phe Met Met Gly 130 135 140

Pro Ile Val Thr Ser Gly Leu Gly Met Ala Ser Thr Ser Ile Ile Thr 145 150 155 160

Pro Phe Ala Ile Ser Val Ala Leu Ser Leu Ile Ala Val Val Gly 165 170 175

Phe Ala Leu Gly Asp Ala Arg Ser Thr Pro Ser Ala Leu Gly Ala Ser 180 185 190

Ser Gly Ile Lys His Glu Arg Ser Met Lys Lys Ala Leu Ala Val Ser 195 200 205

Leu Pro Met Ala Ile Trp Val Phe Ser Cys Ile Thr Thr Ser Leu Ile 210 215 220

Val Met Ser Ala Arg Ile Asp Ser Thr Phe Gly Asn Ala Ile Leu Leu 225 230 235 240

Pro Gly Ile Gly Ala Ala Ile Ala Phe Ser Ala Gly Leu Ile Ala Gln 245 250 255

Phe Leu Gly Arg Lys Phe Ala Trp Gly Arg Gly Ser Gly Ile Val Gly

260 265 270

Ala Leu Cys Ala Leu Ala Gly Phe Ala Leu Ala Ala Phe Gly Gly Asp 275 280 285

Ser Ile Pro Val Trp Leu Phe Val Ile Ala Ser Ile Leu Phe Gly Thr 290 295 300

Ala Tyr Gly Leu Cys Leu Arg Glu Gly Leu Leu Ser Ile Glu Thr Tyr 305 310 315 320

Thr Pro Leu Asn Arg Arg Gly Thr Gly Ile Gly Ile Tyr Tyr Val Phe 325 330 335

Thr Tyr Leu Gly Phe Gly Leu Pro Val Leu Leu Asp Ala Leu Leu Pro 340 345 350

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<220>

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gtg ttg atc cgt gaa caa tta gac gta tca agc gtg ctg gtc aac ggc 96 Val Leu Ile Arg Glu Gln Leu Asp Val Ser Ser Val Leu Val Asn Gly

gct ttt ggt att tat gca ctg gga ctt ctt cca agt ttg ctc gca ggc 144 Ala Phe Gly Ile Tyr Ala Leu Gly Leu Pro Ser Leu Leu Ala Gly 35 40

ggt gtg ctt gcc gac cgt ttt ggt gcc cgc atg gtg gta ctc acc gga 192 Gly Val Leu Ala Asp Arg Phe Gly Ala Arg Met Val Val Leu Thr Gly 50 55

ggt gta ctt tct gcg ctt gga aac ctt tct ctt tta gcg ttt cat gat 240 Gly Val Leu Ser Ala Leu Gly Asn Leu Ser Leu Leu Ala Phe His Asp 65 70 75 80

ggt Gly	cci	t tc Se	c ct r Le	c ct u Le 8	u Va	a gga l Gl	a cga y Ara	a tto g Phe	ate Ile 90	e Va	t gg	t cte	g gg u Gl	c gt y Va 9	t gga 1 Gly 5	288
tta Leu	gto Val	gte L Va	c age l Se: 100	r Ala	g gge a Gl	c aco	c gca	a tgg a Trp 105	Ala	g gg a Gl	c aga y Ara	a tte g Lei	g cg i Are	g Gl	a gca y Ala	336
ago Ser	ggc Gly	gto Val	l Thi	a tto r Leo	g gco ı Ala	e ggo a Gly	att / Ile 120	e Ile	cto Lei	g aco	c gco r Ala	ggt a Gly 125	/ Phe	ato e Mei	g atg t Met	384
Gly	ccg Pro 130	Ile	gto Val	g aca l Thr	a agt Ser	ggg Gly 135	Leu	ggg Gly	ato Met	g gcg	g tco s Ser 140	Thr	ago Ser	att Ile	att lle	432
acg Thr 145	ccc Pro	ttt Phe	gco Ala	ata Ile	ago Ser 150	· Val	gcc Ala	ctc Leu	tcg Ser	Cto Lev 155	ı Ile	gcg Ala	gto Val	ggtt Val	gtg Val 160	480
gga Gly	ttt Phe	gcg	ctt Leu	ggc Gly 165	Asp	gcc Ala	cgc Arg	agc Ser	acc Thr 170	Pro	ago Ser	gca Ala	ctt Leu	ggc Gly 175	gca Ala	528
tcc Ser	agc Ser	gga Gly	atc Ile 180	Lys	cac His	gaa Glu	cga Arg	agc Ser 185	atg Met	aaa Lys	aag Lys	gcc Ala	ctc Leu 190	Ala	gtg Val	576
tcc Ser	ttg Leu	ccg Pro 195	atg Met	gca Ala	att Ile	tgg Trp	gtg Val 200	ttc Phe	agc Ser	tgc Cys	atc Ile	acc Thr 205	acc Thr	tcc Ser	ctg Leu	624
atc Ile	gtg Val 210	atg Met	tcc Ser	gcg Ala	cgc Arg	atc Ile 215	gac Asp	tcc Ser	acc Thr	ttc Phe	ggc Gly 220	aac Asn	gcc Ala	att	ctt Leu	672
ctc Leu 225	ccc Pro	gga Gly	atc Ile	ggc Gly	gcg Ala 230	gcg Ala	atc Ile	gcc Ala	ttc Phe	agc Ser 235	gca Ala	ggc Gly	ctg Leu	atc Ile	gca Ala 240	720
caa Gln	ttt Phe	tta Leu	Gly	agg Arg 245	Lys	Phe	Ala	tgg Trp	Gly	Arg	Gly	Ser	Gly	atc Ile 255	Val	768
ggc Gly	gcg Ala	ctg Leu	tgt Cys 260	gcc Ala	ctc Leu	gcg Ala	ggt Gly	ttt Phe 265	gcg Ala	ctg Leu	gca Ala	gct Ala	ttt Phe 270	ggt Gly	ggc Gly	816
gac Asp	Ser	att Ile 275	cca Pro	gtg Val	tgg Trp	Leu	ttc Phe 280	gtt Val	atc Ile	gcc Ala	tcg Ser	atc Ile 285	ctg Leu	ttc Phe	ggc Gly	864
acc of	gca Ala 290	tat Tyr	ggc Gly	ctc Leu	Cys	ctg Leu 295	cgc Arg	gaa (Glu (ggc Gly	ctc Leu	ctc Leu 300	agc Ser	atc Ile	gaa Glu	act Thr	912

tac Tyr 305	acg Thr	cca Pro	ctc Leu	aac Asn	cga Arg 310	cgt Arg	ggc Gly	acc Thr	ggc Gly	atc Ile 315	ggc Gly	atc Ile	tat Tyr	tat Tyr	gtg Val 320	960
ttc Phe	acg Thr	tat Tyr	ttg Leu	gga Gly 325	ttc Phe	ggg Gly	ctg Leu	cca Pro	gtg Val 330	ctt Leu	ctc Leu	gac Asp	gcc Ala	ctc Leu 335	ctc Leu	1008
ccg Pro	cac His	ctt Leu	ggc Gly 340	gcc Ala	tcc Ser	att Ile	ccg Pro	ctg Leu 345	tac Tyr	gcg Ala	ctg Leu	gcg Ala	gcg Ala 350	ctc Leu	gcc Ala	1056
ctt Leu	ggc Gly	tcc Ser 355	gca Ala	gta Val	atc Ile	Arg	ggc Gly 360	gta Val	caa Gln	atc Ile	aag Lys	cgc Arg 365	ggg Gly	tat Tyr	gtg Val	1104
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<212> PRT

<213> Corynebacterium glutamicum

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Ala Phe Gly Ile Tyr Ala Leu Gly Leu Leu Pro Ser Leu Leu Ala Gly 35 40 45

Gly Val Leu Ala Asp Arg Phe Gly Ala Arg Met Val Val Leu Thr Gly 50 $$ \phantom

Gly Val Leu Ser Ala Leu Gly Asn Leu Ser Leu Leu Ala Phe His Asp 65 70 75 80

Gly Pro Ser Leu Leu Val Gly Arg Phe Ile Val Gly Leu Gly Val Gly 85 90 95

Leu Val Val Ser Ala Gly Thr Ala Trp Ala Gly Arg Leu Arg Gly Ala 100 105 110

Ser Gly Val Thr Leu Ala Gly Ile Ile Leu Thr Ala Gly Phe Met Met 115 120 125

Gly Pro Ile Val Thr Ser Gly Leu Gly Met Ala Ser Thr Ser Ile Ile 130 135 140

Thr Pro Phe Ala Ile Ser Val Ala Leu Ser Leu Ile Ala Val Val 145 150 155 160

Gly Phe Ala Leu Gly Asp Ala Arg Ser Thr Pro Ser Ala Leu Gly Ala 170 Ser Ser Gly Ile Lys His Glu Arg Ser Met Lys Lys Ala Leu Ala Val Ser Leu Pro Met Ala Ile Trp Val Phe Ser Cys Ile Thr Thr Ser Leu 200 Ile Val Met Ser Ala Arg Ile Asp Ser Thr Phe Gly Asn Ala Ile Leu 215 Leu Pro Gly Ile Gly Ala Ala Ile Ala Phe Ser Ala Gly Leu Ile Ala 230 Gln Phe Leu Gly Arg Lys Phe Ala Trp Gly Arg Gly Ser Gly Ile Val 250 Gly Ala Leu Cys Ala Leu Ala Gly Phe Ala Leu Ala Ala Phe Gly Gly 265 Asp Ser Ile Pro Val Trp Leu Phe Val Ile Ala Ser Ile Leu Phe Gly Thr Ala Tyr Gly Leu Cys Leu Arg Glu Gly Leu Leu Ser Ile Glu Thr Tyr Thr Pro Leu Asn Arg Arg Gly Thr Gly Ile Gly Ile Tyr Tyr Val 310 Phe Thr Tyr Leu Gly Phe Gly Leu Pro Val Leu Leu Asp Ala Leu Leu Pro His Leu Gly Ala Ser Ile Pro Leu Tyr Ala Leu Ala Ala Leu Ala 340 345 Leu Gly Ser Ala Val Ile Arg Gly Val Gln Ile Lys Arg Gly Tyr Val 360 365 Val <210> 165

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			gcc Ala												144
		-	cca Pro	-		-	_	-	-			-	_	_	192
			aaa Lys												240
_			aag Lys			_	_		-	-	-	_			288
			aag Lys 100												336
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<211> 113

<212> PRT

<213> Corynebacterium glutamicum

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Ala Asp Thr Gly His Leu Ala Glu Leu Arg Glu Pro Leu Gly Ile Ile 20 25 30

Asp Val Glu Ala Gly Lys Val Asp Arg Met Ile Glu Gln Ala Ala Gly 35 40 45

His Leu Lys Pro Val Gly Glu Arg Asp Leu Val Glu Phe Glu Met Leu 50 55 60

Leu Asp Gln Lys Ser Ile Ala Ser Gln Ile Gly Met Ser Pro Ser Ala 65 70 75 80

Arg His Ile Lys Pro Glu Ala Leu Ala Glu Arg Ile Ala Ala Leu Pro

Glu Gln Met Lys Val Thr Ala Arg Ala Lys Ile Thr Arg Leu Glu Arg 100 105 110

Ile

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att ttc gct gac acc aga ccg ctg aaa gaa ccg gcc ttc aaa cgc ctc lie Phe Ala Asp Thr Arg Pro Leu Lys Glu Pro Ala Phe Lys Arg Leu 10 15 20 ctg ctg gcc aat gtg gcc acc gtc att ggc caa tta act gtt gtt Trp Leu Gly Asn Val Ala Thr Val ile Gly Ala Gln Leu Thr Val Val 25 30 gcc gtt ccg gtg cag att tac caa atg act ggg tcc tcc ggc tat gtg Ala Val Pro Val Gln lle Tyr Gln Met Thr Gly Ser Ser Gly Tyr Val 40 45 50 gcc ttg acc ggg ctt ttt ggc ctt att cct ttg gtt att ttt ggc ctt att ggg ttg acc ggg ttg acc ggg ctt ttt ggc ctt att cct ttg gtt att ttt ggc ctt att ggt gga tca acc ggg tcc tcc ggc tat gtg leu Thr Gly Leu Phe Gly Leu Ile Pro Leu Val Ile Phe Gly Leu 55 60 60 65 scc ggt ttt ttg gat aaa cgc acc gtg ctg acc acc acc gcc ggt ttt ttg gat acc gg gt gct ttt ggt acc acc acc acc acc acc acc acc acc ac	-	-		acca	cago	cg t	tgtc	agcç	ià că	gette	ggtct	; gto	jgagg	gatc	gccg	gaggtta	60
teg ctt gac act ggc cag att tac caa atg act ggt gtc tcc ggc tat gtg ggc ttg acc ggg ctt ttt ggc ctt att cct ttg gtt att ttt ggc ctt act ggt gga tcc att gcg gat gct ttt gat aca cgc atc gtg ttt gat ggc ttg acc ggg ctt ttt ggc ctt att cct ttg gtt att ttt ggc ctt Gly Leu Thr Gly Leu Phe Gly Leu Ile Pro Leu Val Ile Phe Gly Leu 55 tat ggt gga tcc att gcg gat gct ttt gat aaa cgc atc gtg ctg atc Tyr Gly Gly Ser Ile Ala Asp Ala Phe Asp Lys Arg Ile Val Leu Ile 70 acc act tta ggc aat gat ttg gtc acc act gcc ggt ttt tgg gtg ctg Cys Thr Thr Ile Gly Met Cys Val Thr Thr Ala Gly Phe Trp Val Leu 90 acc att tta ggc aat gag aat att tgg ctc ctg tta ata acc ttt ctt Thr Ile Leu Gly Asn Glu Asn Ile Trp Leu Leu Leu Ile Asn Phe Ser 105 tta cag cag gca ttt ttc gcg gtg aat caa ccc acc cga acg gcg atc Leu Gln Gln Ala Phe Phe Ala Val Asn Gln Pro Thr Arg Thr Ala Ile 120 ctt cga agt att ttg ccg att gat caa tta gcg tcg gca aca tca ctg Cys acc act act att tta gcg att gat caa tta gcg tcg gca aca tca ctg Cya agt att ttg ccg att gat caa tta gcg tcg gca aca tca ctg Cya agt att ttc cyc att gat caa tta gcg tcg gca aca tca ctg Cya agt att ttg ccg att gat caa tta gcg tcg gca aca tca ctg Cya agt att ttg ccg att gat caa tta gcg tcg gca aca tca ctg Cya agt att ttg ccg att gat caa tta gcg tcg gca aca tca ctg Cya agt att ttg ccg att gat caa tta gcg tcg gca aca tca ctg Cya agt att ttg ccg att gat caa tta gcg tcg gca aca tca ctg Cya agt att ttg ccg att gat caa tta gcg tcg gca aca tca ctg Cya agt att ttg ccg att gat caa tta gcg tcg gca aca tca ctg Cya agt att ttg ccg att gat caa tta gcg tcg gca aca tca ctg Cya arg Ser Ile Leu Pro Ile Asp Gln Leu Ala Ser Ala Thr Ser Leu	cta	acaa	ata	ggco	caac	aa a	ıgagg	rtcta	ıa go	ctcta	cctg	Val	. Ser			Asp	115
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Ala Val Pro Val Gln Ile Tyr Gln Met Thr Gly Ser Ser Gly Tyr Val 40 45 Gly Leu Thr Gly Leu Phe Gly Leu Ile Pro Leu Val Ile Phe Gly Leu 55 tat ggt gga tcc att gcg gat gct ttt gat aaa cgc atc gtg ctg atc Tyr Gly Gly Ser Ile Ala Asp Ala Phe Asp Lys Arg Ile Val Leu Ile 70 75 Ala Phe Cys Val Thr Thr Ala Gly Phe Trp Val Leu 90 acc att tta ggc aat gag aat att ttg ctc ctg tta ata aac ttt tct Thr Ile Leu Gly Asn Glu Asn Ile Trp Leu Leu Leu Ile Asn Phe Ser 105 tta cag cag gca ttt ttc gcg gtg aat caa ccc acc cga acg gcg atc 499 Ctt cga agt att ttg ccg att gat caa tta gcg tcg gca aca tca ctg Ctt cga agt att ttg ccg att gat caa tta gcg tcg gca aca tca ctg Ctt cga agt att ttg ccg att gat caa tta gcg tcg gca aca tca ctg Ctt cga agt att ttg ccg att gat caa tta gcg tcg gca aca tca ctg Ctt cga agt att ttg ccg att gat caa tta gcg tcg gca aca tca ctg Ctt cga agt att ttg ccg att gat caa tta gcg tcg gca aca tca ctg Ctt cga agt att ttg ccg att gat caa tta gcg tcg gca aca tca ctg Ctt cga agt att ttg ccg att gat caa tta gcg tcg gca aca tca ctg Ctt cga agt att ttg ccg att gat caa tta gcg tcg gca aca tca ctg Ctt cga agt att ttg ccg att gat caa tta gcg tcg gca aca tca ctg Ctt cga agt att ttg ccg att gat caa tta gcg tcg gca aca tca ctg Ctt cga agt att ttg ccg att gat caa tta gcg tcg gca aca tca ctg Ctt cga agt att ttg ccg att gat caa tta gcg tcg gca aca tca ctg Ctt cga agt att ttg ccg att gat caa tta gcg tcg gca aca tca ctg Ctt cga agt att ttg ccg att gat caa tta gcg tcg gca aca tca ctg Ctt cga agt att ttg ccg att gat caa tta gcg tcg gca aca tca ctg	tgg Trp	ctt Leu	ggc Gly	Asn	Val	gcc Ala	acc Thr	gtc Val	Ile	Gly	gcc Ala	caa Gln	tta Leu	Thr	Val	gtt Val	211
Gly Leu Thr Gly Leu Phe Gly Leu Ile Pro Leu Val Ile Phe Gly Leu 55 60 60 65 65 65 65 60 65 65 60 65 65 60 65 65 60 65 65 60 65 65 65 60 65 65 65 60 65 65 60 65 65 60 65 65 60 65 65 65 60 65 60 65 65 60 65 60 65 65 60	gcc Ala	gtt Val	Pro	Val	cag Gln	att Ile	tac Tyr	Gln	Met	act Thr	Gly	tcc Ser	Ser	Gly	tat Tyr	gtg Val	259
Tyr Gly Gly Ser Ile Ala Asp Ala Phe Asp Lys Arg Ile Val Leu Ile 70 75 80 80 85 tgc acc acg atc ggc atg tgt gtc acc act gcc ggt ttt tgg gtg ctg Cys Thr Thr Ile Gly Met Cys Val Thr Thr Ala Gly Phe Trp Val Leu 90 95 100 acc att tta ggc aat gag aat att tgg ctc ctg tta ata aac ttt tct Thr Ile Leu Gly Asn Glu Asn Ile Trp Leu Leu Leu Ile Asn Phe Ser 105 110 115 tta cag cag gca ttt ttc gcg gtg aat caa ccc acc cga acg gcg atc Leu Gln Gln Ala Phe Phe Ala Val Asn Gln Pro Thr Arg Thr Ala Ile 120 125 130 ctt cga agt att ttg ccg att gat caa tta gcg tcg gca aca tca ctg Leu Arg Ser Ile Leu Pro Ile Asp Gln Leu Ala Ser Ala Thr Ser Leu		Leu					Gly					Val	Ile				307
Cys Thr Thr Ile Gly Met Cys Val Thr Thr Ala Gly Phe Trp Val Leu 90 95 100 100 acc att tta ggc aat gag aat att tgg ctc ctg tta ata aac ttt tct 451 Thr Ile Leu Gly Asn Glu Asn Ile Trp Leu Leu Leu Ile Asn Phe Ser 105 110 115 115 tta cag cag gca ttt ttc gcg gtg aat caa ccc acc cga acg gcg atc Leu Gln Gln Ala Phe Phe Ala Val Asn Gln Pro Thr Arg Thr Ala Ile 120 125 130 130 ctt cga agt att ttg ccg att gat caa tta gcg tcg gca aca tca ctg 547 Leu Arg Ser Ile Leu Pro Ile Asp Gln Leu Ala Ser Ala Thr Ser Leu	Tyr	ggt Gly	gga Gly	tcc Ser	att Ile	Ala	gat Asp	gct Ala	ttt Phe	gat Asp	Lys	cgc Arg	atc Ile	gtg Val	ctg Leu	Ile	355
Thr Ile Leu Gly Asn Glu Asn Ile Trp Leu Leu Leu Ile Asn Phe Ser 105 110 115 tta cag cag gca ttt ttc gcg gtg aat caa ccc acc cga acg gcg atc Leu Gln Gln Ala Phe Phe Ala Val Asn Gln Pro Thr Arg Thr Ala Ile 120 125 130 ctt cga agt att ttg ccg att gat caa tta gcg tcg gca aca tca ctg 547 Leu Arg Ser Ile Leu Pro Ile Asp Gln Leu Ala Ser Ala Thr Ser Leu	tgc Cys	acc Thr	acg Thr	atc Ile	Gly	atg Met	tgt Cys	gtc Val	acc Thr	Thr	gcc Ala	ggt Gly	ttt Phe	tgg Trp	Val	ctg Leu	403
Leu Gln Gln Ala Phe Phe Ala Val Asn Gln Pro Thr Arg Thr Ala Ile 120 125 130 ctt cga agt att ttg ccg att gat caa tta gcg tcg gca aca tca ctg Leu Arg Ser Ile Leu Pro Ile Asp Gln Leu Ala Ser Ala Thr Ser Leu	acc Thr	att Ile	Leu	Gly	Asn	Glu	Asn	Ile	Trp	Leu	Leu	Leu	Ile	Asn	Phe	tct Ser	451
Leu Arg Ser Ile Leu Pro Ile Asp Gln Leu Ala Ser Ala Thr Ser Leu	tta Leu	Gln	Gln	gca Ala	ttt Phe	ttc Phe	gcg Ala	Val	aat Asn	caa Gln	ccc Pro	acc Thr	Arg	acg Thr	gcg Ala	atc Ile	499
	Leu	Arg	agt Ser	att Ile	ttg Leu	ccg Pro	Ile	gat Asp	caa Gln	tta Leu	gcg Ala	Ser	gca Ala	aca Thr	tca Ser	ctg Leu	547

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ggt Gly	gcg Ala	tte Lei	g ati u Ile	e Pro	Leu	g ato 11e	ggt Gly	ttc Phe	ggg Gly 175	Trp	g cto Lev	g tat 1 Tyr	ttc Phe	ctt Leu 180	gat Asp	643
gtt Val	gtc Val	tco Sea	2 ato 116 185	: Ile	ccc Pro	aca Thr	ctg Leu	tgg Trp 190	Ala	gta Val	tg <u>c</u> Trp	tca Ser	Leu 195	Pro	tcg Ser	691
ato	aag Lys	Pro 200	Ser	ggc Gly	aag Lys	gtg Val	atg Met 205	Lys	gct Ala	ggt Gly	ttc Phe	gcc Ala 210	Ser	gtg Val	gtg Val	739
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												gct Ala				1027
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gca Ala	gtt Val	cga Arg	aac Asn 345	gct Ala	att Ile	ttg Leu	Gln	cag Gln 350	tct Ser	gct Ala	gcg Ala	gaa Glu	cat His 355	gtg Val	cag Gln	1171
ggc Gly	Arg	atc Ile 360	caa Gln	ggt Gly	gtg Val	Trp	atc Ile 365	atc Ile	gtc Val	gtg Val	gtg Val	ggt Gly 370	gga Gly	cct Pro	cgt Arg	1219
tta	gct	gac	gtc	ctt	cac	ggt	tgg (gcc	gct	gag	ccc	ctc	ggc	gca	ggt	1267

Leu Ala Asp Val Leu His Gly Trp Ala Ala Glu Pro Leu Gly Ala Gly 375 \$380\$

tgg acg gta tta tgg ggc gga gta gcg gtg gtt gta ctc act gca att 1315 Trp Thr Val Leu Trp Gly Gly Val Ala Val Val Val Leu Thr Ala Ile 390 395 400 405

tgt atg gtg gtg cct aaa ttc tgg aaa tac gag aaa cca aaa att 1363 Cys Met Val Ala Val Pro Lys Phe Trp Lys Tyr Glu Lys Pro Lys Ile 410 415 420

acc ggc atc taaatactta tccatgccca ttt 1395
Thr Gly Ile

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<212> PRT

<213> Corynebacterium glutamicum

<400> 168

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35 40 45

Ser Ser Gly Tyr Val Gly Leu Thr Gly Leu Phe Gly Leu Ile Pro Leu 50 55 60

Val Ile Phe Gly Leu Tyr Gly Gly Ser Ile Ala Asp Ala Phe Asp Lys 65 70 75 80

Arg Ile Val Leu Ile Cys Thr Thr Ile Gly Met Cys Val Thr Thr Ala 85 90 95

Gly Phe Trp Val Leu Thr Ile Leu Gly Asn Glu Asn Ile Trp Leu Leu 100 105 110

Leu Ile Asn Phe Ser Leu Gln Gln Ala Phe Phe Ala Val Asn Gln Pro 115 120 125

Thr Arg Thr Ala Ile Leu Arg Ser Ile Leu Pro Ile Asp Gln Leu Ala 130 135 140

Ser Ala Thr Ser Leu Asn Met Leu Leu Met Gln Thr Gly Ala Ile Val 145 150 155 160

Gly Pro Leu Ile Ala Gly Ala Leu Ile Pro Leu Ile Gly Phe Gly Trp 165 170 175

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Phe Ala Ser Val Val Asp Gly Leu Lys Tyr Leu Ala Gly Gln Pro Val 210 215 220

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Asp Ala Gly Ala Thr Met Leu Ala Phe Met Tyr Ser Ser Met Ala Val260 265 270

Gly Ala Val Leu Gly Gly Val Leu Ser Gly Trp Val Ala Arg Ile Ser 275 280 285

Arg Gln Gly Val Ala Val Tyr Trp Cys Ile Ile Ala Trp Gly Ala Ala 290 295 300

Val Ala Leu Gly Gly Val Ala Ile Val Val Ser Pro Gly Ala Val Thr 305 310 315 320

Ala Trp Ala Trp Met Phe Ile Ile Met Met Val Ile Gly Gly Met Ala 325 330 335

Asp Met Phe Ser Ser Ala Val Arg Asn Ala Ile Leu Gln Gln Ser Ala 340 345 350

Ala Glu His Val Gln Gly Arg Ile Gln Gly Val Trp Ile Ile Val Val 355 360 365

Val Gly Gly Pro Arg Leu Ala Asp Val Leu His Gly Trp Ala Ala Glu 370 375 380

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PCT/IB00/00922

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	gtt Val															259
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Ala	Phe	Tuc				.	~ `									
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Gln	Leu		20					25					30	Gly Thr		
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		tcc Ser														883
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		atc Ile 280														979
		gca Ala														1027
		agc Ser														1075
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- Ala Ala Tyr Ala Thr Ile Gly Ile Ala Asn Ala Phe Thr Thr Pro Val 100 105 110
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- Ala Leu Gly Thr Tyr Ala Ala Met Gln Ser Leu Gly Met Leu Ser Ala 130 135 140
- Pro Leu Ile Ala Gly Val Ser Ser Val Val Ser Trp Arg Leu Thr Phe 145 150 155 160
- Leu Val Thr Ala Ala Ala Ser Leu Phe Ile Leu Val Ala Arg Leu Pro 165 170 175
- Val Val Pro Pro Pro Ser Ala Ser Lys Gln Asn Val Ser Gly Lys Val 180 185 190
- Gln Trp Gly Pro Thr Ile Ile His Met Val Ser Gly Phe Val Val Gly 195 200 205
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- Gln Phe Gly Leu Asp Ala Ala Ala Arg Gly Leu Val Val Met Cys Gly 235 230 235
- Gly Leu Ala Ala Phe Phe Ala Ser Arg Lys Ile Gly Asp Leu Ala Asp 245 250 255
- Lys Phe Gly Val Arg Ala Val Leu Ile Val Ser Ala Val Ile Gly Thr 260 265 270
- Ile Ala Leu Ala Leu Leu Pro Ile Ala Pro Trp Ile Ile Val Val Ala

	•	. • • •		•												· • • • • • • • • • • • • • • • • • • •
		275					280	ł				285	i			
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Val 305		Leu	Ala	Val	Ile 310		Ser	Pro	Gly	Gly 315		Ser	Leu	Leu	Ser 320	
Thr	Val	Gln	Ala	Phe 325	Arg	Phe	Phe	Gly	Ser 330		Ala	Ala	Pro	Val 335		
Phe	Leu	Pro	Ile 340	Tyr	Met	Gly	Ile	Gly 345		Gly	Ala	Phe	Trp 350		Ser	
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				gtc Val												211
				gcg Ala												259
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55

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cgt Arg	gaq g Glu	g ctt Leu 120	ı Val	. cc	g cco	g cgt Arç	tct Ser 125	r Lei	g ggt ı Gly	t aaq y Lys	g gca s Ala	ttg Leu 130	GJ À	aco Thr	tat Tyr	499
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Lys Ile His Pro His Lys Val Val Gln Ala Ala Tyr Ile Val Thr Leu 65 70 75 80

Pro Leu Ala Leu Leu Leu Val Thr Pro Ser Trp Gly Leu Phe Met 85 90 95

Ala Ala Tyr Ala Thr Ile Gly Ile Ala Asn Ala Phe Thr Thr Pro Val 100 105 110

Leu Gln Ile Met Leu Arg Glu Leu Val Pro Pro Arg Ser Leu Gly Lys 115 120 125

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Leu Val Thr Ala Ala Ala Ser Leu Phe Ile Leu Val Ala Arg Leu Pro 165 170 175

Val Val Pro Pro Pro Ser Ala Leu Lys Gln Asn Val Ser Gly Lys Val 180 185 190

Gln Trp Gly Pro Thr Ile Ile His Met Val Ser Gly Phe Val Val Gly 195 200 205

Ile Gly Ile Ile Gly Ile Gly Phe Met Thr Ser Leu His Val Gly Glu 210 215 220

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200 205 210

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caa Gln 310	gcc Ala	att Ile	gct Ala	gtc Val	gat Asp 315	tca Ser	gtt Val	cca Pro	agc Ser	act Thr 320	cag Gln	gtt Val	ggt Gly	tcc Ser	ggt Gly 325	1075
att Ile	tct Ser	acg Thr	ctt Leu	ttc Phe 330	ctg Leu	ttc Phe	acc Thr	gac Asp	atc Ile 335	ggc Gly	att Ile	ggc Gly	tta Leu	ggc Gly 340	cca Pro	1123
atc Ile	ctg Leu	ctg Leu	ggt Gly 345	gga Gly	ttg Leu	gtt Val	gca Ala	gcg Ala 350	acc Thr	gga Gly	tac Tyr	aac Asn	gtc Val 355	atg Met	tac Tyr	1171
gca Ala	gct Ala	ttg Leu 360	gcc Ala	gca Ala	gtg Val	Ile	gtt Val 365	gtg Val	gcg Ala	ggc Gly	Val	ctc Leu 370	tac Tyr	ctg Leu	gtt Val	1219
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<211> 381

<212> PRT

<213> Corynebacterium glutamicum

<400> 178

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20 25 30

Val Ser Glu Ala Ala Val Gly Phe Ala Ala Ser Ser Phe Val Ile Gly 35 40 45

Ala Thr Val Ala Arg Val Phe Ala Gly Trp Thr Ser Asp Arg Phe Gly 50 60

Lys Lys Gln Ile Leu Leu Ile Phe Val Gly Leu Glu Ala Val Ala Ser 65 70 75 80

Leu Phe Tyr Ile Pro Ala Ala Ser Leu Pro Ala Leu Val Ala Val Arg 85 90 95

Phe Val His Gly Phe Ser Tyr Ser Leu Ala Ser Thr Ala Val Met Ala 100 105 110

Leu Val Gln Ser Val Ile Pro Ala Ser Arg Arg Ala Glu Gly Thr Gly
115 120 125

Tyr Phe Ala Leu Gly Ser Thr Leu Ala Thr Ala Phe Gly Pro Ala Ile 130 135 140

Ala Leu Phe Val Ile Asp Asp Phe Asn Tyr Asn Thr Leu Phe Trp Ile 145 150 155 . 160

Thr Thr Ala Thr Ser Val Phe Gly Leu Ile Leu Thr Val Leu Ile Arg 165 170 175

Lys Pro Glu Phe Ile Lys Asn Ala Glu His Gly Arg Val Lys Pro Val 180 185 190

Trp Ser Ile Lys Thr Val Val His Pro Ser Val Met Leu Ile Gly Phe 195 200 205

Phe Met Leu Ala Val Gly Leu Ala Tyr Ala Gly Val Ile Thr Phe Leu 210 215 220

Asn Gly Phe Ala Gln Asp Thr Gly Leu Thr Ala Gly Ala Gly Leu Phe 225 230 235 240

Phe Ile Ala Tyr Ala Val Ala Met Leu Val Met Arg Phe Phe Leu Gly 245 250 255

Arg Ile Gln Asp Lys His Gly Asp Asn Pro Val Ile Tyr Phe Gly Leu 260 265 270

Ile Ser Phe Ala Leu Ala Leu Gly Leu Met Ala Leu Ala Thr Glu Asp 275 280 285

Trp His Ile Val Leu Ala Gly Ala Leu Thr Gly Leu Gly Tyr Gly Thr 290 295 300

Ile Met Pro Ala Ala Gln Ala Ile Ala Val Asp Ser Val Pro Ser Thr 305 310 315 320

Gln Val Gly Ser Gly Ile Ser Thr Leu Phe Leu Phe Thr Asp Ile Gly

325 330 335

Ile Gly Leu Gly Pro Ile Leu Leu Gly Gly Leu Val Ala Ala Thr Gly
340 345 350

Tyr Asn Val Met Tyr Ala Ala Leu Ala Ala Val Ile Val Val Ala Gly 355 360 365

Val Leu Tyr Leu Val Ala Leu Gly Arg Lys Ala Ser His 370 375 . 380

<210> 179

<211> 914

<212> DNA

<213> Corynebacterium glutamicum

<220>

<221> CDS

<222> (1)..(891)

<223> FRXA01150

<400> 179

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Phe Ser Tyr Ser Leu Ala Ser Thr Ala Val Met Ala Leu Val Gln Ser
20 25 30

gtg att cct gca agc cgt agg gca gag ggc acc ggc tac ttc gcg ctc 144 Val Ile Pro Ala Ser Arg Arg Ala Glu Gly Thr Gly Tyr Phe Ala Leu 35 40

gga tcc aca ctg gct aca gct ttc ggc cca gca att gcg ctg ttt gtt 192 Gly Ser Thr Leu Ala Thr Ala Phe Gly Pro Ala Ile Ala Leu Phe Val 50 55

atc gat gac ttc aac tac aac acc ctg ttc tgg att acc act gcg acc 240 Ile Asp Asp Phe Asn Tyr Asn Thr Leu Phe Trp Ile Thr Thr Ala Thr 65 70 75 80

agt gtt ttc ggc ctg atc ctc acc gtt ttg atc cgc aag ccg gag ttc 288 Ser Val Phe Gly Leu Ile Leu Thr Val Leu Ile Arg Lys Pro Glu Phe 85 90 95

att aag aat gcg gaa cac ggc aga gta aag cca gtc tgg tct atc aag 336 Ile Lys Asn Ala Glu His Gly Arg Val Lys Pro Val Trp Ser Ile Lys 100 105 110

act gtt gtg cac cca tcg gtc atg ctc att gga ttc ttc atg ctc gct 384
Thr Val Val His Pro Ser Val Met Leu Ile Gly Phe Phe Met Leu Ala
115 120 125

gtc gga ctg gct tac gca ggc gtg atc acc ttc ctc aac ggc ttc gcg 432 Val Gly Leu Ala Tyr Ala Gly Val Ile Thr Phe Leu Asn Gly Phe Ala

135 140 130 caa gac act ggc etc acc gcc gga gcg ggt ett tte ttt atc get tat Gln Asp Thr Gly Leu Thr Ala Gly Ala Gly Leu Phe Phe Ile Ala Tyr gcg gtt gcg atg ctg gtc atg cgt ttc ttc ctt gga cgc att cag gac Ala Val Ala Met Leu Val Met Arg Phe Phe Leu Gly Arg Ile Gln Asp 165 170 aaa cat ggt gac aac ccg gtt att tac ttc ggt ttg atc agc ttc gcc 576 Lys His Gly Asp Asn Pro Val Ile Tyr Phe Gly Leu Ile Ser Phe Ala 180 185 ctc qcq ctq qqq ctt atg qct ttg gcg act gaa gac tgg cac att gtt 624 Leu Ala Leu Gly Leu Met Ala Leu Ala Thr Glu Asp Trp His Ile Val 200 ctc gct ggc gca ctc acc ggt ttg ggc tat ggc acc atc atg ccg gcc 672 Leu Ala Gly Ala Leu Thr Gly Leu Gly Tyr Gly Thr Ile Met Pro Ala 215 gca caa gcc att gct gtc gat tca gtt cca agc act cag gtt ggt tcc Ala Gln Ala Ile Ala Val Asp Ser Val Pro Ser Thr Gln Val Gly Ser 230 768 ggt att tet acg ett tte etg tte ace gae ate gge att gge tta gge Gly Ile Ser Thr Leu Phe Leu Phe Thr Asp Ile Gly Ile Gly Leu Gly 245 cca atc ctg ctg ggt gga ttg gtt gca gcg acc gga tac aac gtc atg 816 Pro Ile Leu Leu Gly Gly Leu Val Ala Ala Thr Gly Tyr Asn Val Met tac gca gct ttg gcc gca gtg att gtt gtg gcg ggc gtg ctc tac ctg Tyr Ala Ala Leu Ala Ala Val Ile Val Val Ala Gly Val Leu Tyr Leu 275 280 285 gtt gct ttg ggt agg aaa gct agc cac taagttagag cattttattg 911 Val Ala Leu Gly Arg Lys Ala Ser His agc 914 <210> 180 <211> 297 <212> PRT <213> Corynebacterium glutamicum <400> 180 Pro Ala Ala Ser Leu Pro Ala Leu Val Ala Val Arg Phe Val His Gly Phe Ser Tyr Ser Leu Ala Ser Thr Ala Val Met Ala Leu Val Gln Ser

25

Val Ile Pro Ala Ser Arg Arg Ala Glu Gly Thr Gly Tyr Phe Ala Leu 35 40 45

- Gly Ser Thr Leu Ala Thr Ala Phe Gly Pro Ala Ile Ala Leu Phe Val 50 55 60
- Ile Asp Asp Phe Asn Tyr Asn Thr Leu Phe Trp Ile Thr Thr Ala Thr 65 70 75 80
- Ser Val Phe Gly Leu Ile Leu Thr Val Leu Ile Arg Lys Pro Glu Phe 85 90 95
- Ile Lys Asn Ala Glu His Gly Arg Val Lys Pro Val Trp Ser Ile Lys
 100 105 110
- Thr Val Val His Pro Ser Val Met Leu Ile Gly Phe Phe Met Leu Ala 115 120 125
- Val Gly Leu Ala Tyr Ala Gly Val Ile Thr Phe Leu Asn Gly Phe Ala 130 135 140
- Gln Asp Thr Gly Leu Thr Ala Gly Ala Gly Leu Phe Phe Ile Ala Tyr 145 150 155 160
- Ala Val Ala Met Leu Val Met Arg Phe Phe Leu Gly Arg Ile Gln Asp 165 170 175
- Lys His Gly Asp Asn Pro Val Ile Tyr Phe Gly Leu Ile Ser Phe Ala 180 185 190
- Leu Ala Leu Gly Leu Met Ala Leu Ala Thr Glu Asp Trp His Ile Val 195 200 205
- Leu Ala Gly Ala Leu Thr Gly Leu Gly Tyr Gly Thr Ile Met Pro Ala 210 215 220
- Ala Gln Ala Ile Ala Val Asp Ser Val Pro Ser Thr Gln Val Gly Ser 225 230 . 235 240
- Gly Ile Ser Thr Leu Phe Leu Phe Thr Asp Ile Gly Ile Gly Leu Gly 245 250 255
- Pro Ile Leu Cly Cly Leu Val Ala Ala Thr Cly Tyr Asn Val Met 260 265 270
- Tyr Ala Ala Leu Ala Ala Val Ile Val Val Ala Gly Val Leu Tyr Leu 275 280 285
- Val Ala Leu Gly Arg Lys Ala Ser His 290 295
- <210> 181
- <211> 1341
- <212> DNA
- <213> Corynebacterium glutamicum

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Ile	Ala	Val	. Val		Met	Туг	Phe	Lys 190		Ser	Asp	Pro	Glu 195		Ser	
			Ala					Lys		att : Ile			Pro		atc Ile	739
		Ile					Leu			_		Ala			ggc Gly	787
	Ile									gaa Glu 240	Arg					835
										gta Val						883
										cgc Arg						931
								-		tcc Ser	_	_		_		979
										tcc Ser						1027
										cag Gln 320						1075
										ttc Phe						1123
										att Ile						1171
tct Ser	gcg Ala	gca Ala 360	att Ile	ggt Gly	ttc Phe	gga Gly	cct Pro 365	atg Met	tat Tyr	gca Ala	gca Ala	ctg Leu 370	gca Ala	ggt Gly	gtg Val	1219
										aca Thr						1267
cga Arg 390	gct Ala	aag Lys	aat Asn	Gly	ttt Phe 395	gtt Val	aaa Lys	cac His	cca Pro	gag Glu 400	cct Pro	gtc Val	gct Ala	tta Leu	gtt Val 405	1315
agc Ser	tagt	tctt	tc a	gctt	tccc	t cc	С									1341

<210> 182

<211> 406

<212> PRT

<213> Corynebacterium glutamicum

<400> 182

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Gly Trp Phe Ala Asn Leu Phe Gln Phe Leu Val Phe Tyr Phe Leu Ile 20 25 30

Thr Thr Met Ala Leu Tyr Ala Ile Lys Glu Phe Gln Ala Ser Glu Val 35 40 45

Glu Ala Gly Phe Ala Ser Ser Ser Ile Val Ile Gly Ala Val Phe Ser 50 55 60

Arg Phe Phe Ser Gly Tyr Ile Ile Asp Arg Phe Gly Arg Arg Lys Ile 65 70 75 80

Val Leu Ile Ser Val Leu Val Thr Thr Ile Ala Cys Ala Leu Tyr Leu 85 90 95

Pro Ile Glu Ser Leu Pro Leu Leu Tyr Ala Asn Arg Phe Leu His Gly
100 105 110

Val Gly Tyr Ala Phe Ala Ala Thr Ala Ile Met Ala Met Val Gln Glu 115 120 125

Leu Ile Pro Ala Ser Arg Arg Ser Glu Gly Thr Gly Tyr Leu Ala Leu 130 135 140

Gly Thr Thr Val Ser Ala Ala Leu Gly Pro Ala Leu Ala Leu Phe Val 145 150 155 160

Leu Gly Thr Phe Asp Tyr Asp Met Leu Phe Ile Val Val Leu Ala Thr 165 170 175

Ser Val Ile Ser Leu Ile Ala Val Val Phe Met Tyr Phe Lys Thr Ser 180 185 190

Asp Pro Glu Pro Ser Gly Glu Pro Ala Lys Phe Ser Phe Lys Ser Ile 195 200 205

Met Asn Pro Lys Ile Ile Pro Ile Gly Ile Phe Ile Leu Leu Ile Cys 210 215 220

Phe Ala Tyr Ser Gly Val Ile Ala Tyr Ile Asn Ala Phe Ala Glu Glu 225 230 235 240

Arg Asp Leu Ile Thr Gly Ala Gly Leu Phe Phe Ile Ala Tyr Ala Val 245 250 255

Ser Met Phe Val Met Arg Ser Phe Leu Gly Lys Leu Gln Asp Arg Arg Gly Asp Asn Val Val Ile Tyr Phe Gly Leu Phe Phe Phe Val Ile Ser 280 Leu Thr Ile Leu Ser Phe Ala Thr Ser Asn Trp His Val Val Leu Ser Gly Val Ile Ala Gly Leu Gly Tyr Gly Thr Leu Met Pro Ala Val Gln Ser Ile Ala Val Gly Val Val Asp Lys Thr Glu Phe Gly Thr Ala Phe Ser Thr Leu Phe Leu Phe Val Asp Leu Gly Phe Gly Pro Ile 345 Ile Leu Gly Ala Val Ser Ala Ala Ile Gly Phe Gly Pro Met Tyr Ala 360 Ala Leu Ala Gly Val Gly Val Ile Ala Gly Ile Phe Tyr Leu Phe Thr His Ala Arg Thr Asp Arg Ala Lys Asn Gly Phe Val Lys His Pro Glu Pro Val Ala Leu Val Ser 405 <210> 183 <211> 1006 <212> DNA <213> Corynebacterium glutamicum <220> <221> CDS <222> (101)..(1006) <223> FRXA02116 <400> 183 ttttatatcc tagcaagggt gttgcatgat gcaataaacg tggtagtttg tgttcataac 60 aaaattgcat gatgcaataa tttcgattta aaggagaaca gtg tcc gta gct gaa Val Ser Val Ala Glu 1 gaa ggg aaa ctt ttt aca cca acg ttt gtc atg gga tgg ttt gcc aac Glu Gly Lys Leu Phe Thr Pro Thr Phe Val Met Gly Trp Phe Ala Asn ctt ttc cag ttc ctg gtg ttc tac ttc ctc atc acc acc atg gct ttg 211 Leu Phe Gln Phe Leu Val Phe Tyr Phe Leu Ile Thr Thr Met Ala Leu 25 tac gcc atc aag gaa ttt caa gcc tct gaa gta gaa gct ggc ttc gca 259

Tyr Ala Ile Lys Glu Phe Gln Ala Ser Glu Val Glu Ala Gly Phe Ala tcc agc tca att gtt atc ggc gca gtc ttt tcc agg ttt ttc tcc ggc Ser Ser Ser Ile Val Ile Gly Ala Val Phe Ser Arg Phe Phe Ser Gly tat att att gac cgt ttt ggt cga cgc aag att gtg ctc atc tca gtc Tyr Ile Ile Asp Arg Phe Gly Arg Arg Lys Ile Val Leu Ile Ser Val cta gtc act acc att gcg tgt gcc ttg tac ctt ccc atc gaa tca ttg 403 Leu Val Thr Thr Ile Ala Cys Ala Leu Tyr Leu Pro Ile Glu Ser Leu 90 cca ttg cta tac gca aac agg ttc ctc cac ggt gtt gga tac gct ttt 451 Pro Leu Leu Tyr Ala Asn Arg Phe Leu His Gly Val Gly Tyr Ala Phe 105 110 get gec acc geg atc atg gea atg gtc cag gag etc att eca geg tea 499 Ala Ala Thr Ala Ile Met Ala Met Val Gln Glu Leu Ile Pro Ala Ser 125 130 cga cgt tcc gaa ggt act ggt tac ctg gca ttg ggc act acc gtt tct 547 Arg Arg Ser Glu Gly Thr Gly Tyr Leu Ala Leu Gly Thr Thr Val Ser gca gca ctt gga cca gcc cta gca ctt ttt gtc cta gga aca ttt gat 595 Ala Ala Leu Gly Pro Ala Leu Ala Leu Phe Val Leu Gly Thr Phe Asp 155 tac gac atg ctg ttt atc gtg gtc ttg gca acc tcg gtc atc tct ttg 643 Tyr Asp Met Leu Phe Ile Val Val Leu Ala Thr Ser Val Ile Ser Leu 170 atc gcc gtc gtg ttc atg tac ttt aag acc agc gac cct gag cct tct 691 Ile Ala Val Val Phe Met Tyr Phe Lys Thr Ser Asp Pro Glu Pro Ser 190 ggg gaa cca gcc aag ttc agc ttc aaa tct att atg aac cca aag atc 739 Gly Glu Pro Ala Lys Phe Ser Phe Lys Ser Ile Met Asn Pro Lys Ile atc ccc atc ggc atc ttt atc ttg ctt att tgc ttt gct tac tct ggc 787 Ile Pro Ile Gly Ile Phe Ile Leu Leu Ile Cys Phe Ala Tyr Ser Gly 220 gtc att gcc tac atc aac gca ttt gct gaa gaa cgc gat ctg att acg 835 Val Ile Ala Tyr Ile Asn Ala Phe Ala Glu Glu Arg Asp Leu Ile Thr 240 ggt gct gga ttg ttc ttc att gcc tac gca gta tca atg ttt gtg atg 883 Gly Ala Gly Leu Phe Phe Ile Ala Tyr Ala Val Ser Met Phe Val Met cgc agc ttc ctt ggc aaa ctg cag gac cgt cgc gga gac aac gtc gtt 931 Arg Ser Phe Leu Gly Lys Leu Gln Asp Arg Arg Gly Asp Asn Val Val

1006

265 270 275

att tac ttt gga ttg ttc ttc ttc gtt att tcc ttg acg att ttg tcc 979

Ile Tyr Phe Gly Leu Phe Phe Phe Val Ile Ser Leu Thr Ile Leu Ser
280 285 290

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<211> 302

<212> PRT

<213> Corynebacterium glutamicum

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Thr Thr Met Ala Leu Tyr Ala Ile Lys Glu Phe Gln Ala Ser Glu Val 35 40 45

Glu Ala Gly Phe Ala Ser Ser Ser Ile Val Ile Gly Ala Val Phe Ser 50 55 60

Arg Phe Phe Ser Gly Tyr Ile Ile Asp Arg Phe Gly Arg Arg Lys Ile 65 70 75 80

Val Leu Ile Ser Val Leu Val Thr Thr Ile Ala Cys Ala Leu Tyr Leu 85 90 95

Pro Ile Glu Ser Leu Pro Leu Leu Tyr Ala Asn Arg Phe Leu His Gly 100 105 110

Val Gly Tyr Ala Phe Ala Ala Thr Ala Ile Met Ala Met Val Gln Glu 115 120 125

Leu Ile Pro Ala Ser Arg Arg Ser Glu Gly Thr Gly Tyr Leu Ala Leu 130 135 140

Gly Thr Thr Val Ser Ala Ala Leu Gly Pro Ala Leu Ala Leu Phe Val 145 150 155 160

Leu Gly Thr Phe Asp Tyr Asp Met Leu Phe Ile Val Val Leu Ala Thr 165 170 175

Ser, Val Ile Ser Leu Ile Ala Val Val Phe Met Tyr Phe Lys Thr Ser 180 185 190

Asp Pro Glu Pro Ser Gly Glu Pro Ala Lys Phe Ser Phe Lys Ser Ile 195 200 205

Met Asn Pro Lys Ile Ile Pro Ile Gly Ile Phe Ile Leu Leu Ile Cys

	210)				215	5				220)				
Phe 225	Ala	Туг	Ser	Gly	/ Val 230		e Ala	э Ту:	r Ile	23		a Phe	e Ala	a Glu	Glu 240	
Arg	Asp	Leu	ılle	Thr 245		Ala	a Gly	y Le	u Phe 250		e Ile	e Ala	туг	255	a Val	
Ser	Met	Phe	Val 260		Arg	Ser	Phe	265		/ Ly:	s Leu	Glr	Asp 270	_	, Arg	
Gly	Asp	Asn 275		Val	Ile	Tyr	Phe 280		/ Leu	Phe	e Phe	285		. Ile	Ser	
Leu	Thr 290		Leu	Ser	Phe	Ala 295		Ser	Asr	Trp	300		Val			
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tctt	aaat	tg (tctaa	accaa	agaa	accg	gagg	t tc	tttt	tgtc	atg Met 1				tta Leu 5	115
gcc Ala	aca Thr	tgg Trp	cta Leu	atc Ile 10	act Thr	atc Ile	gca Ala	gtg Val	att Ile 15	gct Ala	gģc Gly	ttc Phe	ttc Phe	att Ile 20	ttc Phe	163
gat Asp	ttc Phe	tat Tyr	tcc Ser 25	cac His	gtc Val	cgc Arg	acc Thr	cca Pro 30	cac His	gag Glu	ccc Pro	act Thr	atc Ile 35	aaa Lys	gaa Glu	211
tcc (Ser /	gca Ala	tgg Trp 40	tgg Trp	agc Ser	ctc Leu	ttc Phe	tac Tyr 45	gta Val	gcc Ala	ctc Leu	gcc Ala	tgt Cys 50	gtt Val	ttc Phe	ggc Gly	259
gtg (/al	ttc Phe 55	ctc Leu	tgg Trp	ttt Phe	gct Ala	tgg Trp 60	ggc Gly	gag Glu	cca Pro	ggt Gly	aac Asn 65	cca Pro	cac His	cag Gln	cac His	307
gc a Sly 1 70	att Ile	gag Glu	ttc Phe	ttc Phe	acc Thr 75	ggt Gly	tac Tyr	gtg Val	aca Thr	gag Glu 80	aag Lys	gcg Ala	ttg Leu	agt Ser	gtt Val 85	355

403

gat aac ctc ttc atc ttc gcg ctg atc atg ggt tct ttc aag att cct Asp Asn Leu Phe Ile Phe Ala Leu Ile Met Gly Ser Phe Lys Ile Pro

90 95 100

cgc aag tac cag cag aag gtt ctg ctc atc ggt atc gcg ctg gca ctg 451 Arg Lys Tyr Gln Gln Lys Val Leu Leu Ile Gly Ile Ala Leu Ala Leu 105 110

gtc ttc cgc ctg gca ttc atc ctc gca ggt gct gca gtt atc gaa gcc 499 Val Phe Arg Leu Ala Phe Ile Leu Ala Gly Ala Ala Val Ile Glu Ala 120 125 130

tgg tcc gat gtc ttc tac atc ttc tcc atc tgg ctg atc tac acc gct 547
Trp Ser Asp Val Phe Tyr Ile Phe Ser Ile Trp Leu Ile Tyr Thr Ala
135 140 145

gtg aag gct cct gtg cac gag 568 Val Lys Ala Pro Val His Glu 150 155

<210> 186

<211> 156

<212> PRT

<213> Corynebacterium glutamicum

<400> 186

Met Glu Val Asn Leu Ala Thr Trp Leu Ile Thr Ile Ala Val Ile Ala 1 5 10 15

Gly Phe Phe Ile Phe Asp Phe Tyr Ser His Val Arg Thr Pro His Glu 20 25 30

Pro Thr Ile Lys Glu Ser Ala Trp Trp Ser Leu Phe Tyr Val Ala Leu $35 \hspace{1.5cm} 40 \hspace{1.5cm} 45$

Ala Cys Val Phe Gly Val Phe Leu Trp Phe Ala Trp Gly Glu Pro Gly 50 55 60

Asn Pro His Gln His Gly Ile Glu Phe Phe Thr Gly Tyr Val Thr Glu 65 70 75 80

Lys Ala Leu Ser Val Asp Asn Leu Phe Ile Phe Ala Leu Ile Met Gly 85 90 95

Ser Phe Lys Ile Pro Arg Lys Tyr Gln Gln Lys Val Leu Leu Ile Gly 100 105 110

Ile Ala Leu Ala Leu Val Phe Arg Leu Ala Phe Ile Leu Ala Gly Ala 115 120 125

Ala Val Ile Glu Ala Trp Ser Asp Val Phe Tyr Ile Phe Ser Ile Trp 130 135 140

Leu Ile Tyr Thr Ala Val Lys Ala Pro Val His Glu 145 150 155

<210> 187

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	<pre><400> 187 tatgcgcgca ggtgtctact ggtgacgcag ccgacgacga ttattttgac gaagccaccg 6(caaacgatga cttcgatccc gaaaagtgga ggaacatgta atg cca gcc ttt gag 11</pre>														g 60	
caa	acga	atga	ctt	cgat	ccc (gaaaa	agtg	ga go	gaaca	atgta		Pro			gag Glu 5	115
gca Ala	ato Met	g cca Pro	a gga o Gly	a ato y Met 10	Pro	g tat Tyr	tgg Trp	g ato	gad Asp	Lev	g tcc ı Ser	aco Thr	tco Ser	gac Asp 20	att Ile	163
gca Ala	aaa Lys	tct Ser	gca Ala 25	a His	tto Phe	tac Tyr	gaa Glu	aac Asn 30	Val	cto Lev	ggc Gly	tgg Trp	gaa Glu 35	Ile	gaa Glu	211
gaa Glu	gto Val	aac Asn 40	Asp	ggc Gly	tac Tyr	cgc Arg	atg Met 45	Ala	cgt Arg	ctg Leu	cag Gln	gga Gly 50	Leu	ccc Pro	gtg Val	259
gca Ala	ggg Gly 55	Leu	ato	gat Asp	cag Gln	cgc Arg 60	Gly	gaa Glu	tca Ser	agc Ser	atc Ile 65	Pro	gat Asp	acc Thr	tgg Trp	307
att Ile 70	acc Thr	tac Tyr	ttc Phe	ctc Leu	tcc Ser 75	tac Tyr	gat Asp	ctg Leu	gat Asp	gcc Ala 80	act Thr	gca Ala	aag Lys	aag Lys	atc Ile 85	355
gca Ala	gaa Glu	ctg Leu	ggt Gly	gga Gly 90	cga Arg	att Ile	ctg Leu	gcc Ala	gag Glu 95	cca Pro	act Thr	gac Asp	gtg Val	cac His 100	ttg Leu	403
gga Gly	cgc Arg	atg Met	atc Ile 105	cta Leu	gct Ala	gtt Val	gat Asp	act Thr 110	gcc Ala	ggc Gly	gca Ala	ctg Leu	ttc Phe 115	ggc Gly	gtt Val	451
att Ile	gag Glu	cca Pro 120	ggc Gly	agc Ser	gag Glu	gaa Glu	tca Ser 125	ttc Phe	gtc Val	gct Ala	gct Ala	ggt Gly 130	gaa Glu	cca Pro	ggc Gly	499
aca Thr	tcc Ser 135	gtg Val	tgg Trp	cat His	gaa Glu	ctc Leu 140	acc Thr	act Thr	gtc Val	tcc Ser	aaa Lys 145	tat Tyr	tcc Ser	gaa Glu	gct Ala	547
le 50	gat Asp	ttc Phe	tac Tyr	ggt Gly	gag Glu 155	ctg Leu	ttc Phe	act Thr	tgg Trp	aca Thr 160	acc Thr	tct Ser	gaa Glu	atg Met	gct Ala 165	595
gt	gct	gaa	gac	gat	agt	ttc	cgc	tac	acc	acc	gca	ttg	gct	gac	ggt	643

Sei	Ala	Glu	ı Asp	Asp 170		Pho	e Arq	J Tyr	Th:		Ala	a Lei	a Ala	Asp 180	Gly	
				Gly					Lys					Pro	cag Gln	691
gtt Val	cca Pro	ago Ser 200	Phe	tgo Tr	g cag Gln	Sei	tac Tyr 205	Leu	ggc Gly	gtg Val	cto Leu	aac Asn 210	Ala	gat Asp	gat Asp	739
					aag Lys		Phe					Ile				787
	Asp				ggc Gly 235						Ser					835
					tgt Cys					Tyr						883
					ttc Phe											931
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Ser	Thr	Ser	Asp 20		Ala	-		2 5		Phe	_		20		Leu	
Gly	Trp	Glu 35	Ile	Glu	Glu	Val	Asn 40	Asp	Gly	Tyr	Arg	Met 45	Ala	Arg	Leu	
Gln	Gly 50	Leu	Pro	Val	Ala	Gly 55	Leu	Ile	Asp	Gln	Arg 60	Gly	Glu	Ser	Ser	
Ile 65	Pro	Asp	Thr	Trp	Ile 70	Thr	Tyr	Phe	Leu	Ser 75	Tyr	Asp	Leu	Asp	Ala 80	
Thr	Ala	Lys	Lys	Ile 85	Ala	Glu	Leu	Gly	Gly 90	Arg	Ile	Leu	Ala	Glu 95	Pro	
Thr	Asp	Val	His	Leu	Gly .	Arg	Met	Ile	Leu	Ala	Val	Asp	Thr	Ala	Gly	

100 105 110

Ala Leu Phe Gly Val Ile Glu Pro Gly Ser Glu Glu Ser Phe Val Ala 115 120 125

Ala Gly Glu Pro Gly Thr Ser Val Trp His Glu Leu Thr Thr Val Ser 130 135 140

Lys Tyr Ser Glu Ala Ile Asp Phe Tyr Gly Glu Leu Phe Thr Trp Thr 145 150 155 160

Thr Ser Glu Met Ala Ser Ala Glu Asp Asp Ser Phe Arg Tyr Thr Thr 165 170 175

Ala Leu Ala Asp Gly Ser Ala Phe Ala Gly Ile Phe Asp Ala Lys Gly 180 185 190 .

His Phe Pro Pro Gln Val Pro Ser Phe Trp Gln Ser Tyr Leu Gly Val 195 200 205

Leu Asn Ala Asp Asp Ala Ala Ala Lys Ala Lys Glu Phe Gly Gly Asp 210 215 220

Val Ile Arg Lys Pro Trp Asp Ser Glu Phe Gly Arg Met Val Leu Ile 225 230 235 240

Ser Asp Ser Thr Gly Ala Thr Ile Thr Leu Cys Glu Val Glu Glu Tyr 245 250 255

Val Glu Glu Ala Ala Glu Gly Asp Asp Leu Phe Asp Ile Asp Leu Ser 260 265 270

Ala Phe Glu Glu Gln Phe Arg Lys Gln Glu Gly Gln 275 280

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Pro Asp Gln Leu Lys Trp Glu Tyr Ser Ala Phe Pro Val Gln Ile Ser
10 15 20

ca Gl:	g aad n Ly:	g ca s Gl	a cgo n Aro 25	g Le	t ag u Se:	t cco	ggo Gly	c tto y Phe 30	e Met	g cgg	g ato	c aco	gto Val	l Th	t ggt r Gly	211
gad Ası	c aaq c Lys	g cto s Lem 40	ı Arç	a tt g Ph	c tti e Pho	t ggg e Gly	caq Glr 45	Tr	g ggt o Gly	tto Lei	g gad u Asp	caa Glr 50	Arg	c ato	c aaa e Lys	259
cto Lei	ato 1 Ile 55	e Ile	t cca	a ago Se:	c ccq	g gct o Ala 60	Gly	g aac / Asr	ato Ile	cca Pro	gat Asp 65) Phe	gga Gly	a att	ctc Leu	307
gad Asp 70	Glu	rcc Pro	act Thi	Pro	c cca p Pro 75	Pro	aca Thr	acg Thr	tgg Trp	ctt Leu 80	Pro	cgt Arg	gct	aaq Lys	g tct Ser 85	355
ttt Phe	cca Pro	gcg Ala	g gac Asp	caa Glr 90	n Arg	ccg Pro	ato	ttg Leu	cgc Arg 95	Thr	tac Tyr	acc Thr	cca	tct Ser 100	gcg Ala	403
gto Val	cga Arg	Pro	gaa Glu 105	Let	tgc Cys	gaa Glu	gta Val	gac Asp 110	Ile	gat Asp	ato	tat Tyr	ctt Leu 115	His	aac Asn	451
cct Pro	tcg Ser	gga Gly 120	Pro	gta Val	tcc Ser	aga Arg	tgg Trp 125	gca Ala	aag Lys	aac Asn	tgc Cys	agt Ser 130	gtt Val	gac Asp	gat Asp	499
gaa Glu	cta Leu 135	atc Ile	atc Ile	acc Thr	ggc	cct Pro 140	gac Asp	gta Val	cgc Arg	gca Ala	gga Gly 145	gaa Glu	acc Thr	ggc Gly	tac Tyr	547
gga Gly 150	atc Ile	acc Thr	tat Tyr	cat His	ccg Pro 155	act Thr	tct Ser	gcg Ala	atc Ile	gat Asp 160	cgc Arg	ctc Leu	tgt Cys	ctc Leu	atc Ile 165	595
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aaa Lys	gta Val	cct Pro	act Thr 185	acg Thr	gtt Val	ttc Phe	ctc Leu	cac His 190	gta Val	gac Asp	agc Ser	cta Leu	gaa Glu 195	gat Asp	gat Asp	691
gta Val	ttg Leu	atc Ile 200	gcc Ala	gat Asp	agc Ser	Ser	acc Thr 205	aag Lys	ctc Leu	act Thr	ttc Phe	gaa Glu 210	gac Asp	atc Ile	gac Asp	739
gct Ala	tac Tyr 215	aaa Lys	gca Ala	aag Lys	gtc Val	ttc Phe 220	caa Gln	tgg Trp	gct Ala	tca Ser	gcc Ala 225	aat Asn	gca Ala	gca Ala	gat Asp	787
cct Pro 230	tca Ser	gta Val	cac His	ttc Phe	tgg Trp 235	atc Ile .	gcc Ala	ggt Gly	Glu	act Thr 240	agc Ser	atg Met	gtg Val	cgc Arg	ttc Phe 245	835
att	cgc	aaa	gaa	cta	atc	aac a	agc	tac	cga	gtt	gat	tcc	tca	cga	atc	883

Ile Arg Lys Glu Leu Ile Asn Ser Tyr Arg Val Asp Ser Ser Arg Ile 250 255 260

act ttc ctc ggc tac tgg aaa tac ggc cga cga acc gta gac

Thr Phe Leu Gly Tyr Trp Lys Tyr Gly Arg Arg Thr Val Asp
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948

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<211> 275

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<213> Corynebacterium glutamicum

<400> 190

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Pro Val Gln Ile Ser Gln Lys Gln Arg Leu Ser Pro Gly Phe Met Arg 20 25 30

Ile Thr Val Thr Gly Asp Lys Leu Arg Phe Phe Gly Gln Trp Gly Leu 35 40 45

Asp Gln Arg Ile Lys Leu Ile Ile Pro Ser Pro Ala Gly Asn Ile Pro 50 55 60

Asp Phe Gly Ile Leu Asp Glu Pro Thr Pro Pro Pro Thr Thr Trp Leu 65 70 75 80

Pro Arg Ala Lys Ser Phe Pro Ala Asp Gln Arg Pro Ile Leu Arg Thr 85 90 95

Tyr Thr Pro Ser Ala Val Arg Pro Glu Leu Cys Glu Val Asp Ile Asp 100 105 110

Ile Tyr Leu His Asn Pro Ser Gly Pro Val Ser Arg Trp Ala Lys Asn 115 120 125

Cys Ser Val Asp Asp Glu Leu Ile Ile Thr Gly Pro Asp Val Arg Ala 130 135 140

Gly Glu Thr Gly Tyr Gly Ile Thr Tyr His Pro Thr Ser Ala Ile Asp 145 150 . 155 160

Arg Leu Cys Leu Ile Gly Asp Cys Ala Ser Ala Pro Ala Ile Ala Asn 165 170 175

Ile Val Asn Gln Ser Lys Val Pro Thr Thr Val Phe Leu His Val Asp 180 185 190

Ser Leu Glu Asp Asp Val Leu Ile Ala Asp Ser Ser Thr Lys Leu Thr 195 200 205

Phe Glu Asp Ile Asp Ala Tyr Lys Ala Lys Val Phe Gln Trp Ala Ser 210 215 220

Ala Asn Ala Ala Asp Pro Ser Val His Phe Trp Ile Ala Gly Glu Thr 230 Ser Met Val Arg Phe Ile Arg Lys Glu Leu Ile Asn Ser Tyr Arg Val 245 250 Asp Ser Ser Arg Ile Thr Phe Leu Gly Tyr Trp Lys Tyr Gly Arg Arg 265 Thr Val Asp 275 <210> 191 <211> 468 <212> DNA <213> Corynebacterium glutamicum <220> <221> CDS <222> (101)..(445) <223> RXA00843 <400> 191 gccctgatgc gaaaccggcg ccaacaatga tgccgacgaa ggcaaatgcc actcttagga 60 tttgaataat catggaacaa accttagtag gctcaacgtt atg aaa gtc acg att 115 Met Lys Val Thr Ile ttc cat aat ccg cgt tgt tcc aca tcc aga aat acc ctc gct tac ctc 163 Phe His Asn Pro Arg Cys Ser Thr Ser Arg Asn Thr Leu Ala Tyr Leu 15 ege gae aag gae att gag eet gaa att gtt eag tat ete aaa gae aeg 211 Arg Asp Lys Asp Ile Glu Pro Glu Ile Val Gln Tyr Leu Lys Asp Thr ccc acc gct tcc gag ctc aaa gaa cta ttc aat acg ctg gga att cca 259 Pro Thr Ala Ser Glu Leu Lys Glu Leu Phe Asn Thr Leu Gly Ile Pro 4.5 gtc cac gac ggc atc aga acc cgc gaa gct gag tac aca gaa ctg ggc 307 Val His Asp Gly Ile Arg Thr Arg Glu Ala Glu Tyr Thr Glu Leu Gly ctg tca cca gaa aca cct gaa act gag ctt atc gac gcc atc gtt gcc 355 Leu Ser Pro Glu Thr Pro Glu Thr Glu Leu Ile Asp Ala Ile Val Ala cat ccc agg ctc ctt cag cgt ccg atc gtg gtg acg gcc aaa ggc gcg 403 His Pro Arg Leu Leu Gln Arg Pro Ile Val Val Thr Ala Lys Gly Ala 90 cgc att gcg cgc ccc aaa atc gac gtc att gac agc atc ttg 445 Arg Ile Ala Arg Pro Lys Ile Asp Val Ile Asp Ser Ile Leu

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<210> 192

<211> 115

<212> PRT

<213> Corynebacterium glutamicum

<400> 192

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Thr Leu Ala Tyr Leu Arg Asp Lys Asp Ile Glu Pro Glu Ile Val Gln
20 25 30

Tyr Leu Lys Asp Thr Pro Thr Ala Ser Glu Leu Lys Glu Leu Phe Asn 35 40 45

Thr Leu Gly Ile Pro Val His Asp Gly Ile Arg Thr Arg Glu Ala Glu 50 55 60

Tyr Thr Glu Leu Gly Leu Ser Pro Glu Thr Pro Glu Thr Glu Leu Ile
65 70 75 80

Asp Ala Ile Val Ala His Pro Arg Leu Leu Gln Arg Pro Ile Val Val 85 90 95

Thr Ala Lys Gly Ala Arg Ile Ala Arg Pro Lys Ile Asp Val Ile Asp 100 105 110

Ser Ile Leu 115

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ggc gct gaa ttg ggt act gaa ttt gat ctc att gtt ggt ttc ggc 163 Gly Ala Glu Leu Gly Thr Glu Phe Asp Leu Ile Val Val Gly Phe Gly 10 15 20

	-		aag Lys 25				_			_	-				_	211
_	_	_	atc Ile		_	-		_	_					-		259
			tgc Cys													307
	-	-	ttc Phe	-	-		-			-	_	-	_			355
_	-		gcc Ala	_				-	-		-	_		_		403
cgt Arg		tgat	ggaa:	iaa g	ctac	gttt	a ca	ıg								432

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<212> PRT

<213> Corynebacterium glutamicum

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Ala Ala Gly Asp Lys Val Ala Leu Ile Glu Gln Ser Pro Gln Met Tyr 35 40 45

Gly Gly Thr Cys Ile Asn Val Gly Cys Ile Pro Thr Lys Lys Leu Leu 50 55 60

Phe Glu Thr Ala Thr Gly Lys Asp Phe Pro Asp Ala Val Val Ala Arg 65 70 75 80

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Gly	Ile	Gln 35	His	Ile	Ser	Pro	Leu 40		Lys	His	s Leu	Ala 45		e Ile	e Gly	
Gly	Gly 50	Pro	Ile	Gly	Leu	Glu 55	Phe	Ala	Thr	Leu	Phe 60		Gl	/ Glr	Gly	
Ser 65	Lys	Val	Thr	Ile	Ile 70	Asp	Arg	Gly	Glu	Leu 75		Leu	Lys	a Asr	Phe 80	
Asp	Arg	Glu	Val	Ala 85	Glu	Leu	Ala	Lys	Thr 90		Leu	Glu	Ala	Arg	Gly	
Ile	Thr	Phe	Leu 100	Asn	Asn	Ala	Glu	Leu 105	Thr	Gly	Phe	Ser	Gly 110		Leu	
Thr	Ile	Ala 115	Leu	Lys	Asp	His	Asp 120	Leu	Leu	Ala	Asp	Ala 125	Ala	Leu	Phe	
Ala	Ser 130	Ala	Asp	Ala	Arg	His 135	Arg	Arg	Ala	Arg	Pro 140					
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cac d His I	ctc d Leu <i>I</i>	egg a	acc a Thr <i>I</i>	aac a Asn 1	atc (Ile <i>I</i>	gac (Asp (ggc Gly	atc Ile	ttc Phe 15	gct Ala	gta Val	ggt Gly	gat Asp	gtc Val 20	aat Asn	163
ggc g	gc o	ccg c	ag t Sln E 25	tt a Phe 1	acc t	ac (Tyr)	gtg : /al :	tcc Ser 30	tac Tyr	gat Asp	gac Asp	cac His /	cgc Arg 35	att Ile	gtg Val	211
etg g Leu A	sp G	aa c ln L 40	ta g eu A	jec ç la G	ga a Sly T	ca c	ggt a Gly I 45	aag a Lys 1	aaa Lys	tcc Ser	att (gca (Ala 1 50	cac His	cga Arg	ctg Leu	259
itc c	сс а	cc a	сс а	cg t	tc a	tc o	aa c	ca a	ca 1	tta ·	tcc a	acc a	atc	aat	gac	307

Ile	e Pro		r Th	r Th	r Ph	e Ile 60		u Pro	o Pro	o Le	u Se:		r Il	e Gl	y Asp	
aad Asi 70	n Thi	t gaa	agg uGl	g ga y Gl	a aar u Asr 7.	n Val	g gte L Val	g gto l Val	g aaa l Lys	a aad s Ly:	s Ala	c tto a Leo	g att	t gc	a gat a Asp 85	
ato Met	g ccc Pro	g ato	c gti e Val	t cc l Pro	o Arg	a cca g Pro	a gaq o Glu	g att ı Ile	t att e Ile 95	e Ası	c caa	a cct	cac His	ggt s Gl ₂	t atg y Met O	403
gtg Val	g aaq Lys	g ttt s Phe	tto Phe 105	∍ Val	c gad L Asp	c aag c Lys	g caa Glr	tct Ser 110	Asp	gco Ala	g cto a Lei	g cto ı Lev	ggc Gl ₃ 115	/ Ala	g acc a Thr	451
ttg Lev	tac Tyr	tgc Cys 120	: Ala	gad Asp	c tco Ser	cag Gln	gag Glu 125	Leu	ato Ile	aac Asr	aco Thr	gtg Val	Ala	ctt Leu	gec Ala	499
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l Val	Gly	Asp		5 Asn	Gly	Gly	Pro		10 Phe	Thr	Tyr	Val		15 Tyr	Asp	
Asp	His	Arg 35	20 Ile	Val	Leu	Asp	Gln 40	25 Leu	Ala	Gly	Thr	Gly 45	30 Lys	Lys	Ser	
Ile	Ala 50	His	Arg	Leu	Ile	Pro 55	Thr	Thr	Thr	Phe	Ile 60	Glu	Pro	Pro	Leu	
Ser 65	Thr	Ile	Gly	Asp	Asn 70	Thr	Glu	Gly	Glu	Asn 75	Val	Val	Val	Lys	Lys 80	
Ala	Leu	Ile	Ala	Asp 85	Met	Pro	Ile	Val	Pro 90	Arg	Pro	Glu	Ile	Ile 95	Asn	
Gln	Pro	His'	Gly 100	Met	Val	Lys		Phe 105	Val	Asp	Lys	Gln	Ser 110	Asp	Ala	

Leu Leu Gly Ala Thr Leu Tyr Cys Ala Asp Ser Gln Glu Leu Ile Asn 120 Thr Val Ala Leu Ala Met Arg His Gly Val Thr Ala Ser Glu Leu Gly 135 Asp Gly Ile Tyr Thr His Pro Ala Thr Ser Glu Ile Phe Asn Gln Leu 150 155 Leu Gly Ser <210> 199 <211> 561 <212> DNA <213> Corynebacterium glutamicum <220> <221> CDS <222> (101)..(538) <223> RXN03123 <400> 199 agetetacea aegegeetae acettgacea aegtggatge egatgeeggt acetttgace 60 tggcttttgt gctgcacgag ccgctggggc ccgcctcggc gtg ggc gac gcg ctg 115 Val Gly Asp Ala Leu cga ggc cgg gga aag cct gaa gtc atg cgc tac cca gga att ccg ttc Arg Gly Arg Gly Lys Pro Glu Val Met Arg Tyr Pro Gly Ile Pro Phe 10 15 20 gcc atc cca gat cca gcg ccg cgt ggc ttc ctt ttc tta ggc gat ctc 211 Ala Ile Pro Asp Pro Ala Pro Arg Gly Phe Leu Phe Leu Gly Asp Leu 25 acc tct tac cca gcg atc tgc tcg att ctg gag acc ttg gac ggt gaa 259 Thr Ser Tyr Pro Ala Ile Cys Ser Ile Leu Glu Thr Leu Asp Gly Glu 40 45 atc cct gcg acc gcg tat ctt atc gcc cac gat cca ctt gat tac acc 307 Ile Pro Ala Thr Ala Tyr Leu Ile Ala His Asp Pro Leu Asp Tyr Thr 55 ttc gat ttt ccc cag ggc gag cac atc acc gcg cag tgg att tcc aac 355 Phe Asp Phe Pro Gln Gly Glu His Ile Thr Ala Gln Trp Ile Ser Asn 70 75 gaa caa too tto att gat cac atc got gac acg gat tac acc gat ttt Glu Gln Ser Phe Ile Asp His Ile Ala Asp Thr Asp Tyr Thr Asp Phe 90 100 tat acc tgg atc ggc gcg gaa tcc tcc gaa acc cgt gcg gcc aag aag Tyr Thr Trp Ile Gly Ala Glu Ser Ser Glu Thr Arg Ala Ala Lys Lys 105 110

cat ctg cag acc cac gcc ggc atg ccc aag acg cac atg aac gcg caa 499 His Leu Gln Thr His Ala Gly Met Pro Lys Thr His Met Asn Ala Gln 125 ggt tat tgg aac aag ggc aga gcc atg ggt aaa agc aat taaaagattt Gly Tyr Trp Asn Lys Gly Arg Ala Met Gly Lys Ser Asn 135 140 ttgcttatcg acg 561 <210> 200 <211> 146 <212> PRT <213> Corynebacterium glutamicum Val Gly Asp Ala Leu Arg Gly Arg Gly Lys Pro Glu Val Met Arg Tyr Pro Gly Ile Pro Phe Ala Ile Pro Asp Pro Ala Pro Arg Gly Phe Leu Phe Leu Gly Asp Leu Thr Ser Tyr Pro Ala Ile Cys Ser Ile Leu Glu Thr Leu Asp Gly Glu Ile Pro Ala Thr Ala Tyr Leu Ile Ala His Asp Pro Leu Asp Tyr Thr Phe Asp Phe Pro Gln Gly Glu His Ile Thr Ala Gln Trp Ile Ser Asn Glu Gln Ser Phe Ile Asp His Ile Ala Asp Thr Asp Tyr Thr Asp Phe Tyr Thr Trp Ile Gly Ala Glu Ser Ser Glu Thr Arg Ala Ala Lys Lys His Leu Gln Thr His Ala Gly Met Pro Lys Thr His Met Asn Ala Gln Gly Tyr Trp Asn Lys Gly Arg Ala Met Gly Lys 140 Ser Asn 145 <210> 201 <211> 736 <212> DNA <213> Corynebacterium glutamicum <220> <221> CDS <222> (101)..(736)

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736

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<211> 212

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<213> Corynebacterium glutamicum

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Val Thr Ile His Phe His Ser Glu Thr Leu Leu Asn Thr Glu Gly Glu 35 40 45

Val Pro Gly Asp Trp Leu Arg Leu Trp Phe Pro His Glu Ser Arg Pro 50 55 60

Gly Lys Leu Tyr Gln Arg Ala Tyr Thr Leu Thr Asn Val Asp Ala Asp 65 70 75 80

Ala Gly Thr Phe Asp Leu Ala Phe Val Leu His Glu Pro Leu Gly Pro 85 90 95

Ala Ser Ala Trp Ala Thr Arg Cys Glu Ala Gly Glu Ser Leu Glu Val 100 105 110

Met Arg Tyr Pro Gly Ile Pro Phe Ala Ile Pro Asp Pro Ala Pro Arg 115 120 125

Gly Phe Leu Phe Leu Gly Asp Leu Thr Ser Tyr Pro Ala Ile Cys Ser 130 135 140

Ile Leu Glu Thr Leu Asp Gly Glu Ile Pro Ala Thr Ala Tyr Leu Ile 145 150 155 160

Ala His Asp Pro Leu Asp Tyr Thr Phe Asp Phe Pro Gln Gly Glu His 165 170 175

Ile Thr Ala Gln Trp Ile Ser Asn Glu Gln Ser Phe Ile Asp His Ile 180 185 190

Ala Asp Thr Asp Tyr Thr Asp Phe Tyr Thr Trp Ile Gly Ala Glu Ser 195 200 205

Ser Glu Thr Arg 210

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gga gca tcc gta gca gcg ctt gtc tcg ctt aaa tcc tcc aag gta gtc Gly Ala Ser Val Ala Ala Leu Val Ser Leu Lys Ser Ser Lys Val Val 170

155

150

160

agc gga atc atc atg ggc ggt tca cta tct gtg atg gcg atg atg atg 691 Ser Gly Ile Ile Met Gly Gly Ser Leu Ser Val Met Ala Met Met Met 185 190 195

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Tyr Ser Ser Phe Ile Ala
200

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<212> PRT

<213> Corynebacterium glutamicum

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Gly Ser His His Ala Pro Pro Gln Lys Asp Glu Ser Val Lys Lys Ser 20 25 30

Phe Asn Ala Ser Ser Leu Leu Phe Ala Phe Ser Phe Gly Val Tyr Leu 35 40 45

Val Leu Leu Val Met Met Thr Leu Leu Lys Ser Arg Leu Ser Leu Gly 50 60

Gly Leu Trp Asn Thr Glu Ala His Gln Tyr Arg Ser Ile Asp Leu Glu 65 70 .75 80

Leu Phe Asn Gly Phe Ala Asp Pro Pro Ile Trp Trp Gly Pro Trp Thr 85 90 95

Asn Thr Phe Gly Asn Ile Ala Leu Phe Met Pro Phe Gly Phe Phe Leu 100 105 110

Tyr Lys Met Leu Arg Arg Phe Asn His Arg Phe Pro Phe Val Glu Thr 115 120 125

Ile Leu Phe Ala Ser Val Thr Ser Leu Ser Ile Glu Val Leu Gln Trp 130 135 140

Val Phe Ala Ile Gly Tyr Ser Asp Val Asp Asp Leu Leu Phe Asn Thr 145 150 155 160

Ile Gly Gly Leu Ile Gly Ala Ser Val Ala Ala Leu Val Ser Leu Lys 165 170 175

Ser Ser Lys Val Val Ser Gly Ile Ile Met Gly Gly Ser Leu Ser Val 180 185 190

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Gl	y Gl	y Le	u Th	r Gl 17		g Me	t Il	e Pr	o Al 17		y Le	u Lei	u Gli	u Va 18	l Thr O	
ca Hi	t tg s Tr	g ca p Gl	a aa n As 18	n Al	a cto a Leo	g ct u Le	g gg u Gl	a agt y Sei 190	r Se	t ate	c gct e Ala	t gco	g cto Let 195	1 Il	c ttc e Phe	691
gg Gl	c gta y Val	a at 1 Il 20	e Me	g gt t Va	g gte l Val	g tte	g cti u Lei 20!	ı Pro	c aad b Lys	g cad S Gli	g egg n Arg	g aaa g Lys 210	s Phe	c cade Glu	g ccg n Pro	739
aaq Lys	g aat s Asr 215	ı Il	c aa e Ası	t ct	g cgo u Aro	cat g His 220	s Glu	g att i Ile	tce Ser	g gcg Ala	g ato Met 225	: Ala	gct Ala	cat His	t tgg s Trp	787
cgg Arg 230	, Asr	cct Pro	cgi Arq	t tto	g gcg ı Ala 235	Let	g ctt 1 Leu	ttt Phe	ggt Gly	act Thr 240	Ala	ttt Phe	ttg Leu	ggo Gly	atg Met 245	835
ggt Gly	act Thr	ttt Phe	gto Val	tco Sei 250	: Leu	tac	aac Asn	tat Tyr	ttg Leu 255	Gly	ttc Phe	cgc Arg	atg Met	att 11e 260	gat Asp	883
cag Gln	ttt Phe	ggg	cto Leu 265	Ser	gaa Glu	gtg Val	ctg Leu	gtt Val 270	Gly	gcg	gtg Val	ttc Phe	atc Ile 275	Met	tat Tyr	931
ctg Leu	gcc Ala	999 Gly 280	Thr	tgg Trp	agt Ser	tcc Ser	acc Thr 285	cag Gln	gcg Ala	ggt Gly	gcg Ala	ttg Leu 290	agg Arg	gag Glu	aag Lys	979
atc Ile	ggc Gly 295	aat Asn	Gly	tca Ser	acg Thr	gtt Val 300	att Ile	ttc Phe	ttg Leu	agt Ser	ctg Leu 305	acg Thr	atg Met	atc Ile	gcg Ala	1027
tcg Ser 310	atg Met	gca Ala	ctg Leu	atg Met	ggg Gly 315	att Ile	aat Asn	aat Asn	ttg Leu	tgg Trp 320	gtc Val	acg Thr	ttg Leu	gtt Val	gcc Ala 325	1075
ctg Leu	ttt Phe	gtg Val	ttt Phe	acc Thr 330	gcg Ala	gca Ala	ttt Phe	ttc Phe	gca Ala 335	ctg Leu	cat His	tcc Ser	agt Ser	gct Ala 340	tcg Ser	1123
gga Gly	tgg Trp	atc Ile	gga Gly 345	atc Ile	atc Ile	gca Ala	acg Thr	aag Lys 350	gat Asp	cgc Arg	gcg Ala	gaa Glu	gcc Ala 355	tcc Ser	agc Ser	1171
atg Met	tat Tyr	ttg Leu 360	ttc Phe	tgt Cys	tat Tyr	tac Tyr	gtg Val 365	gga Gly	tcc Ser	tcg Ser	gtg Val	att Ile 370	ggt Gly	tgg Trp	gtt Val	1219
tct Ser	gga Gly 375	ttc Phe	gcg Ala	ttt Phe	acg Thr	cat His 380	ttg Leu	ccg Pro	tgg Trp	ttg Leu	gcg Ala 385	ttc Phe	att Ile	ggc Gly	tgg Trp	1267
ttg Leu	att Ile	ctg Leu	ctt Leu	ctt Leu	tgc Cys	gga Gly	gtg Val	ctg Leu	gcg Ala	att Ile	tgt Cys	gtg Val	acg Thr	ctg Leu	gca Ala	1315

1359

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agg ctt gcc cgc aac gcc aat taatacgagt ttgtccgtgt tta Arg Leu Ala Arg Asn Ala Asn 410

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<211> 412

<212> PRT

<213> Corynebacterium glutamicum

<400> 206

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Gly His Glu Gly Ile Glu Arg Gly Thr Arg Asn Tyr Lys Arg Ala Val 20 25 30

Phe Ala Met Leu Ala Ala Gly Leu Ala Ala Phe Asn Gly Leu Tyr Cys $35 \hspace{1cm} 40 \hspace{1cm} 45$

Thr Gln Ala Leu Leu Pro Thr Met Thr Glu Glu Leu Gly Ile Thr Pro 50 55

Thr Glu Ser Ala Leu Thr Val Ser Ala Thr Thr Gly Met Leu Ala Leu 65 70 75 80

Cys Ile Val Pro Ala Ser Ile Leu Ser Glu Lys Phe Gly Arg Gly Arg 85 90 95

Val Leu Thr Ile Ser Leu Thr Leu Ala Ile Ile Val Gly Leu Ile Leu 100 105 110

Pro Leu Val Pro Asn Ile Thr Ala Leu Ile Leu Leu Arg Gly Leu Gln 115 120 125

Gly Ala Leu Leu Ala Gly Thr Pro Ala Val Ala Met Thr Trp Leu Ser 130 135 140

Glu Glu Ile His Pro Lys Asp Ile Gly His Ala Met Gly Ile Tyr Ile 145 150 155 160

Ala Gly Asn Thr Val Gly Gly Leu Thr Gly Arg Met Ile Pro Ala Gly 165 170 175

Leu Leu Glu Val Thr His Trp Gln Asn Ala Leu Leu Gly Ser Ser Ile 180 185 190

Ala Ala Leu Ile Phe Gly Val Ile Met Val Val Leu Leu Pro Lys Gln 195 200 205

Arg Lys Phe Gln Pro Lys Asn Ile Asn Leu Arg His Glu Ile Ser Ala 210 . 215 220

Met Ala Ala His Trp Arg Asn Pro Arg Leu Ala Leu Leu Phe Gly Thr 225 230 235 240

Ala Phe Leu Gly Met Gly Thr Phe Val Ser Leu Tyr Asn Tyr Leu Gly 245 Phe Arg Met Ile Asp Gln Phe Gly Leu Ser Glu Val Leu Val Gly Ala 265 Val Phe Ile Met Tyr Leu Ala Gly Thr Trp Ser Ser Thr Gln Ala Gly 280 Ala Leu Arg Glu Lys Ile Gly Asn Gly Ser Thr Val Ile Phe Leu Ser Leu Thr Met Ile Ala Ser Met Ala Leu Met Gly Ile Asn Asn Leu Trp 315 Val Thr Leu Val Ala Leu Phe Val Phe Thr Ala Ala Phe Phe Ala Leu His Ser Ser Ala Ser Gly Trp Ile Gly Ile Ile Ala Thr Lys Asp Arq Ala Glu Ala Ser Ser Met Tyr Leu Phe Cys Tyr Tyr Val Gly Ser Ser Val Ile Gly Trp Val Ser Gly Phe Ala Phe Thr His Leu Pro Trp Leu Ala Phe Ile Gly Trp Leu Ile Leu Leu Leu Cys Gly Val Leu Ala Ile 390 Cys Val Thr Leu Ala Arg Leu Ala Arg Asn Ala Asn <210> 207 <211> 1215 <212> DNA <213> Corynebacterium glutamicum <220> <221> CDS <222> (101)..(1192) <223> FRXA01873 <400> 207 ccgtcgttgc ccatggtcac agcctacatg cacaaagtga atcaaaaaca gctatttcta 60 acattttact aatatttgct gttggcgcat gatgaactcc atg agc caa gca ata Met Ser Gln Ala Ile gat age aag gte gag gea cae gaa gge cae gaa gge cae gaa gge ate Asp Ser Lys Val Glu Ala His Glu Gly His Glu Gly His Glu Gly Ile 10 gag cga gga aca cgc aat tac aag cgc gct gtg ttt gcg atg ctg gcc

Glu Arg Gly Thr Arg Asn Tyr Lys Arg Ala Val Phe Ala Met Leu Ala gcc ggt ctt gct gct ttc aat ggt ctt tat tgc acg cag gca ttg ctt 259 Ala Gly Leu Ala Ala Phe Asn Gly Leu Tyr Cys Thr Gln Ala Leu Leu 45 ccc acc atg acg gaa gag ttg gga att acg ccc act gag tcc gcg ctg 307 Pro Thr Met Thr Glu Glu Leu Gly Ile Thr Pro Thr Glu Ser Ala Leu acg gtg tcg gct acg act gga atg ttg gcg ctg tgt att gtt ccg gcg 355 Thr Val Ser Ala Thr Thr Gly Met Leu Ala Leu Cys Ile Val Pro Ala tcq ata ctt tcg gag aaa ttt ggt cgc ggt cgg gtg ctg aca att tca 403 Ser Ile Leu Ser Glu Lys Phe Gly Arg Gly Arg Val Leu Thr Ile Ser ctc acg ttg gcc atc atc gtg gga tta att ttg ccg ctt gtc ccc aat 451 Leu Thr Leu Ala Ile Ile Val Gly Leu Ile Leu Pro Leu Val Pro Asn 110 att act gct ctc atc ctg ctc aga ggt ctc caa ggt gcg ctg ctt gct 499 Ile Thr Ala Leu Ile Leu Leu Arg Gly Leu Gln Gly Ala Leu Leu Ala 125 ggc act cca gcg gtg gcg atg acc tgg ttg tct gag gaa att cac ccc 547 Gly Thr Pro Ala Val Ala Met Thr Trp Leu Ser Glu Glu Ile His Pro 140 aag gat att ggg cat gcg atg gga att tac atc gcg gga aat act gtc 595 Lys Asp Ile Gly His Ala Met Gly Ile Tyr Ile Ala Gly Asn Thr Val 155 160 ggc ggg ctc act gga cgt atg att ccg gcg gga cta ctt gaa gta act 643 Gly Gly Leu Thr Gly Arg Met Ile Pro Ala Gly Leu Leu Glu Val Thr 170 cat tgg caa aac gca ctg ctg gga agt tct atc gct gcg ctg atc ttc 691 His Trp Gln Asn Ala Leu Leu Gly Ser Ser Ile Ala Ala Leu Ile Phe 190 ggc gta atc atg gtg gtg ttg ctt ccc aag cag cgg aaa ttc cag ccg 739 Gly Val Ile Met Val Val Leu Leu Pro Lys Gln Arg Lys Phe Gln Pro 205 aag aat atc aat ctg cgc cat gag att tcg gcg atg gct gct cat tgg 787 Lys Asn Ile Asn Leu Arg His Glu Ile Ser Ala Met Ala Ala His Trp 220 cgg aat cct cgt ttg gcg ttg ctt ttt ggt act gcg ttt ttg ggc atg 835 Arg Asn Pro Arg Leu Ala Leu Leu Phe Gly Thr Ala Phe Leu Gly Met 235 ggt act ttt gtg tcg ctg tac aac tat ttg ggt ttc cgc atg att gat 883 Gly Thr Phe Val Ser Leu Tyr Asn Tyr Leu Gly Phe Arg Met Ile Asp

250 255 260 cag ttt ggg ctg agt gaa gtg ctg gtt ggt gcg gtg ttc atc atg tat 931 Gln Phe Gly Leu Ser Glu Val Leu Val Gly Ala Val Phe Ile Met Tyr 270 ctg gcc ggg acc tgg agt tcc acc cag gcg ggt gcg ttg agg gag aag 979 Leu Ala Gly Thr Trp Ser Ser Thr Gln Ala Gly Ala Leu Arg Glu Lys 285 atc ggc aat ggg tca acg gtt att ttc ttg agt ctg acg atg atc gcg 1027 Ile Gly Asn Gly Ser Thr Val Ile Phe Leu Ser Leu Thr Met Ile Ala 295 300 tog atg gca ctg atg ggg att aat aat ttg tgg gtc acg ttg gtt gcc 1075 Ser Met Ala Leu Met Gly Ile Asn Asn Leu Trp Val Thr Leu Val Ala 315 320 ctg ttt gtg ttt acc gcg gca ttt ttc gca ctg cat tcc agt gct tcg 1123 Leu Phe Val Phe Thr Ala Ala Phe Phe Ala Leu His Ser Ser Ala Ser 330 335 gga tgg atc gga atc atc gca acg aag gat cgc gcg gaa gcc tcc agc 1171 Gly Trp Ile Gly Ile Ile Ala Thr Lys Asp Arg Ala Glu Ala Ser Ser atg tat ttg ttc tgt gaa tac taggatcctc ggtgattggt tgg 1215 Met Tyr Leu Phe Cys Glu Tyr 360 <210> 208 <211> 364 <212> PRT <213> Corynebacterium glutamicum <400> 208 Met Ser Gln Ala Ile Asp Ser Lys Val Glu Ala His Glu Gly His Glu 10 Gly His Glu Gly Ile Glu Arg Gly Thr Arg Asn Tyr Lys Arg Ala Val Phe Ala Met Leu Ala Ala Gly Leu Ala Ala Phe Asn Gly Leu Tyr Cys 40

Thr Gln Ala Leu Leu Pro Thr Met Thr Glu Glu Leu Gly Ile Thr Pro

Thr Glu Ser Ala Leu Thr Val Ser Ala Thr Thr Gly Met Leu Ala Leu 70

Cys Ile Val Pro Ala Ser Ile Leu Ser Glu Lys Phe Gly Arg Gly Arg

Val Leu Thr Ile Ser Leu Thr Leu Ala Ile Ile Val Gly Leu Ile Leu 100

Pro Leu Val Pro Asn Ile Thr Ala Leu Ile Leu Leu Arg Gly Leu Gln 115 120 125

- Gly Ala Leu Leu Ala Gly Thr Pro Ala Val Ala Met Thr Trp Leu Ser 130 140
- Glu Glu Ile His Pro Lys Asp Ile Gly His Ala Met Gly Ile Tyr Ile 145 150 155 160
- Ala Gly Asn Thr Val Gly Gly Leu Thr Gly Arg Met Ile Pro Ala Gly 165 170 175
- Ala Ala Leu Ile Phe Gly Val Ile Met Val Val Leu Leu Pro Lys Gln 195 200 205
- Arg Lys Phe Gln Pro Lys Asn Ile Asn Leu Arg His Glu Ile Ser Ala 210 215 220
- Met Ala Ala His Trp Arg Asn Pro Arg Leu Ala Leu Leu Phe Gly Thr 225 230 235 240
- Ala Phe Leu Gly Met Gly Thr Phe Val Ser Leu Tyr Asn Tyr Leu Gly 245 250 255
- Phe Arg Met Ile Asp Gln Phe Gly Leu Ser Glu Val Leu Val Gly Ala 260 265 270
- Val Phe Ile Met Tyr Leu Ala Gly Thr Trp Ser Ser Thr Gln Ala Gly 275 280 285
- Ala Leu Arg Glu Lys Ile Gly Asn Gly Ser Thr Val Ile Phe Leu Ser 290 295 300
- Leu Thr Met Ile Ala Ser Met Ala Leu Met Gly Ile Asn Asn Leu Trp 305 310 315 320
- Val Thr Leu Val Ala Leu Phe Val Phe Thr Ala Ala Phe Phe Ala Leu 325 330 335
- His Ser Ser Ala Ser Gly Trp Ile Gly Ile Ile Ala Thr Lys Asp Arg 340 345 350
- Ala Glu Ala Ser Ser Met Tyr Leu Phe Cys Glu Tyr 355 360
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Ala Ile Ala Leu Thr Arg His Ile Pro Glu Ser Arg Pro Ala Gln Ser

			His					Gly					ıÁla		agt Ser	739
gtt Val	cta Leu 215	Sei	ctt Lei	gaa Glu	tto Lev	ttt Phe 220	Ile	acc Thr	caa Gln	ggt Gly	gaa Glu 225	ı Ser	ctt Leu	ggc Gly	tgg Trp	787
acg Thr 230	His	tgg Trp	ato Met	g acc	tgg Trp 235	Thr	Leu	ctt Leu	gcc Ala	gtt Val 240	Ser	ttg Leu	aca Thr	ttt Phe	ctt Leu 245	835
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				Lys					Ser			acc Thr				931
ttc Phe	att Ile	atg Met 280	Ser	gct Ala	act Thr	ggc Gly	gga Gly 285	gta Val	gtt Val	gcc Ala	gtt Val	gtc Val 290	atg Met	tgg Trp	gtt Val	979
Gln	Gln 295	Met	Gly	Trp	Gly	Val 300	Ser	Pro	Thr	Ile	Ser 305	gga Gly	Leu	Thr	Ser	1027
atc Ile 310	ggc Gly	ttc Phe	gca Ala	gcc Ala	ttt Phe 315	gtc Val	atc Ile	ctt Leu	ttc Phe	att Ile 320	cga Arg	gtt Val	gga Gly	gaa Glu	aag Lys 325	1075
Ala	Met	Gln	Lys	Val 330	Gly	Ala	Arg	Ala	Val 335	Ile	Ile	acc Thr	Ala	Gly 340	Ile	1123
Leu	Val	Ala	Thr 345	Ala	Thr	Ala	Leu	Leu 350	Met	Ile	Thr	gcg Ala	Val 355	Ser	Glu	1171
Ser	Thr	Tyr 360	Ile	Val	Ile	Ser	Leu 365	Ala	Gly	Phe	Ser	ctt Leu 370	Tyr	Gly	Leu	1219
Gly	Leu 375	Gly	Leu	Phe	Ala	Thr 380	Pro	Val	Thr	Asp	Thr 385	gcg Ala	Leu	Gly	Thr	1267
Leu 390	Pro	Lys	Asp	Arg	Thr 395	Gly	Ala	Gly	Ala	Gly 400	Val	ttc Phe	Lys	Met	Ser 405	1315
tct Ser	tcc Ser	ctc Leu	ggc Gly	gca Ala 410	gca Ala	ctc Leu	ggc Gly	Ile	gca Ala 415	atc Ile	tcc Ser	act Thr	tca Ser	gtg Val 420	ttc Phe	1363

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Ile Val Ser Ile Val Ala Ile Ala Leu Thr Arg His Ile Pro Glu Ser 180 185 190

- Arg Pro Ala Gln Ser Ile Gly Met His Leu Asp Trp Ser Gly Ile Ile 195 200 205
- Val Leu Ala Leu Ser Val Leu Ser Leu Glu Leu Phe Ile Thr Gln Gly 210 215 220
- Glu Ser Leu Gly Trp Thr His Trp Met Thr Trp Thr Leu Leu Ala Val 225 230 235 240
- Ser Leu Thr Phe Leu Ala Val Phe Val Phe Ile Glu Arg Ile Ala Ser 245 250 255
- Trp Pro Val Leu Asp Phe Asn Leu Phe Lys Asp His Ala Phe Ser Gly 260 265 270
- Ala Thr Ile Thr Asn Phe Ile Met Ser Ala Thr Gly Gly Val Val Ala 275 280 285
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- Ser Gly Leu Thr Ser Ile Gly Phe Ala Ala Phe Val Ile Leu Phe Ile 305 310 315 320
- Arg Val Gly Glu Lys Ala Met Gln Lys Val Gly Ala Arg Ala Val Ile 325 330 335
- Ile Thr Ala Gly Ile Leu Val Ala Thr Ala Thr Ala Leu Leu Met Ile 340 345 350
- Thr Ala Val Ser Glu Ser Thr Tyr Ile Val Ile Ser Leu Ala Gly Phe 355 360 365
- Ser Leu Tyr Gly Leu Gly Leu Gly Leu Phe Ala Thr Pro Val Thr Asp 370 380
- Thr Ala Leu Gly Thr Leu Pro Lys Asp Arg Thr Gly Ala Gly Ala Gly 385 390 395 400
- Val Phe Lys Met Ser Ser Ser Leu Gly Ala Ala Leu Gly Ile Ala Ile 405 410 415
- Ser Thr Ser Val Phe Leu Ala Leu Arg Asp Gly Thr Ser Ile Asn Ser 420 425 430
- Asp Val Ala Leu Ala Gly Thr Val Ser Leu Gly Ile Asn Val Val Phe 435 440 445
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- Gly Lys Val Ser Gln Thr Ser Ile Thr Leu Pro Glu Pro Ala Ile Ala 465 470 475 480

Val Lys Ile

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			Leu			agc Ser										259
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Asn Ile Ala Val Ala Ala Ala Leu Phe Cys Gly Thr Phe Ile Val 50 55 60

Ala Ala Gly Gly Ile Ala Asp Val Phe Gly Arg Val Arg Ile Met Met 65 70 75 80

Ile Gly Asn Ile Leu Asn Ile Leu Gly Ser Leu Leu Ile Ala Thr Ala 85 90 95

Thr Thr Ser Leu Ala Thr Gln Met Val Ile Thr Gly Arg Val Leu Gln 100 105 110

Gly Leu Ala Ala Ala Ile Met Ser Ala Ser Leu Ala Leu Val Lys 115 120 125

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Ile Gly Ser Trp Gly Gly Thr Gly Phe Cys Ala Leu Phe Ala Gly Leu 145 150 155 160

Val Val Ala Ser Pro Phe Gly Trp Arg Gly Ile Phe Ala Leu Cys Ala 165 170 175

Ile Val Ser Ile Val Ala Ile Ala Leu Thr Arg His Ile Pro Glu Ser 180 185 190

Arg Pro Ala Gln Ser Ile Gly Met His Leu Asp Trp Ser Gly Ile Ile 195 200 205

Val Leu Ala Leu Ser Val Leu Ser Leu Glu Leu Phe Ile Thr Gln Gly 210 215 220

Glu Ser Leu Gly Trp Thr His Trp Met Thr Trp Thr Leu Leu Ala Val 225 230 235 240

Ser Leu Thr Phe Leu Ala Val Phe Val Phe Ile Glu Arg Ile Ala Ser 245 250 255

Trp Pro Val Leu Asp Phe Asn Leu Phe Lys Asp His Ala Phe Ser Gly 260 265 270

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Phe Asp Ala Asp Ser Ala Met Asp Ile Ser Ala Glu Asp Arg Glu Lys 175 gtc acc aat att ctt gat gaa tac gat gac ggc gat ctg act gtt gtc 691 Val Thr Asn Ile Leu Asp Glu Tyr Asp Asp Gly Asp Leu Thr Val Val tac aac ggc aac gtg ttt ggc gca gct gca acc agc ttg gac atg acc 739 Tyr Asn Gly Asn Val Phe Gly Ala Ala Ala Thr Ser Leu Asp Met Thr 205 tet gag etc atc gge etg etg gtg get geg gte gtt ett atc gtg acc 787 Ser Glu Leu Ile Gly Leu Leu Val Ala Ala Val Val Leu Ile Val Thr 220 ttc ggt tcg ttc atc gct gcc ggt atg ccg ctg atc tct 826 Phe Gly Ser Phe Ile Ala Ala Gly Met Pro Leu Ile Ser 235

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Gly Leu Asp Ser Val Thr Thr Met Glu Lys Met Gln Glu Arg Phe Pro 50 60

Gly Ser Asp Asp Ala Thr Ser Ala Pro Thr Gly Ser Val Val Ile Gln
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Ala Pro Glu Gly Lys Thr Leu Thr Asp Pro Glu Val Gly Ala Glu Val 85 90 95

Asn Gln Met Leu Asp Glu Val Arg Ala Thr Gly Val Leu Lys Asp Ala 100 105 110

Asp Ser Val Val Asp Pro Val Leu Ala Ala Gln Gly Val Ala Ala Gln 115 120 125

Met Thr Pro Ala Leu Glu Ala Gln Gly Val Pro Ala Glu Lys Ile Ala 130 135 140

Ala Asp Ile Glu Ser Ile Ser Pro Leu Ser Ala Asp Glu Thr Thr Gly
145 150 155 160

Ile Ile Ser Met Thr Phe Asp Ala Asp Ser Ala Met Asp Ile Ser Ala

165 170 175

Glu Asp Arg Glu Lys Val Thr Asn Ile Leu Asp Glu Tyr Asp Asp Gly
180 185 190

Asp Leu Thr Val Val Tyr Asn Gly Asn Val Phe Gly Ala Ala Ala Thr 195 200 205

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gtc tgg ctc gtg att ctc ata ggt atc acg acg ctg gcg ggg ctg tat 211
Val Trp Leu Val Ile Leu Ile Gly Ile Thr Thr Leu Ala Gly Leu Tyr
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Ala Lys Pro Thr Ser Ser Ser Phe Ser Ile Pro Gly Leu Asp Ser Val
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90 95 100

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cct Pro	gtg Val	ttg Leu 120	gct Ala	gcg Ala	cag Gln	ggt Gly	gtg Val 125	gct Ala	gct Ala	cag Gln	atg Met	acc Thr 130	cca Pro	gcc Ala	ctg Leu	499
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Tyr	Asn	Gly 200	Asn	Val	ttt Phe	Gly	Ala 205	Ala	Ala	Thr	Ser	Leu 210	Asp	Met	Thr	739
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Gly Leu Asp Ser Val Thr Thr Met Glu Lys Met Gln Glu Arg Phe Pro 55

Gly Ser Asp Asp Ala Thr Ser Ala Pro Thr Gly Ser Val Val Ile Gln 70 Ala Pro Glu Gly Lys Thr Leu Thr Asp Pro Glu Val Gly Ala Glu Val Asn Gln Met Leu Asp Glu Val Arg Ala Thr Gly Val Leu Lys Asp Ala 105 Asp Ser Val Val Asp Pro Val Leu Ala Ala Gln Gly Val Ala Ala Gln Met Thr Pro Ala Leu Glu Ala Gln Gly Val Pro Ala Glu Lys Ile Ala Ala Asp Ile Glu Ser Ile Ser Pro Leu Ser Ala Asp Glu Thr Thr Gly Ile Ile Ser Met Thr Phe Asp Ala Asp Ser Ala Met Asp Ile Ser Ala Glu Asp Arg Glu Lys Val Thr Asn Ile Leu Asp Glu Tyr Asp Asp Gly Asp Leu Thr Val Val Tyr Asn Gly Asn Val Phe Gly Ala Ala Ala Thr Ser Leu Asp Met Thr Ser Glu Leu Ile Gly Leu Leu Val Ala Ala Val 215 Val Leu Ile Val Thr Phe Gly Ser Phe Ile Ala Ala Gly Met Pro Leu 230 235 Ile Ser <210> 217 <211> 2313 <212> DNA <213> Corynebacterium glutamicum <220> <221> CDS <222> (101)..(2290) <223> RXA00479 <400> 217 tagatcccaa ggctcaaaat ttattactta aacaagttga gcaactagcc agccgcaaat 60 cttagaacta acctttacgc ctttaacgga agtgaatttg atg tct act agc atc 115 Met Ser Thr Ser Ile aca aca gag aac aag aag aaa tot ggt cot cot cgc ttg atg aga atc Thr Thr Glu Asn Lys Lys Ser Gly Pro Pro Arg Leu Met Arg Ile 10

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agt Ser	ato	e ego Aro	g Glr	a act	t tti r Phe	gca Ala	a gat a Asp 525	Glu	a aat 1 Asr	ata lle	tca Ser	gcg Ala 530	Val	a gta L Val	ggc Gly	1699
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cgc Arg 550	Asn	cto Lev	ato Ile	ato : Ile	e cca Pro	Ile	gta Val	ttg Leu	ctg Leu	gtc Val 560	Ile	ttg Leu	gtt Val	att	ctc Leu 565	1795
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acc Thr	ctg Leu	ctc Leu	gtt Val	cgc Arg	gcc Ala	ttc Phe	ttg Leu	gtg Val	cct Pro	gct Ala :	ttg Leu	ttc Phe	tac Tyr	gac Asp	atc Ile	2227

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Gly Pro Lys Ile Trp Trp Pro Ser Lys Leu Ser Asn Gln Lys Tyr Gln
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Gln Val Gln Glu Gln Leu Gly Asp Phe Thr Asp Ser Glu Ser Ile Pro 65 70 75 80

Ala Ile Val Val Met Val Ser Asp Glu Pro Leu Thr Gln Gln Asp Ile 85 90 95

Thr Gln Leu Asn Glu Val Val Ala Gly Leu Ser Glu Leu Asp Ile Val 100 105 110

Ser Asp Glu Val Ser Pro Ala Ile Pro Ser Glu Asp Gly Arg Ala Val 115 120 125

Gln Val Phe Val Pro Leu Asn Pro Ser Ala Glu Leu Thr Glu Ser Val 130 135 140

Glu Lys Leu Ser Glu Thr Leu Thr Gln Gln Thr Pro Asp Tyr Val Ser 145 150 155 160

Thr Tyr Val Thr Gly Pro Ala Gly Phe Thr Ala Asp Leu Ser Ala Ala 165 170 175

Phe Ala Gly Ile Asp Gly Leu Leu Leu Ala Val Ala Leu Ala Ala Val 180 185 190

Leu Val Ile Leu Val Ile Val Tyr Arg Ser Phe Ile Leu Pro Ile Ala 195 200 205

Val Leu Ala Thr Ser Leu Phe Ala Leu Thr Val Ala Leu Leu Val Val

210 215 220

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- Glu Lys Ala Arg Ala Lys Asn Asp Ile Pro Ala Ser Gly Ile Trp Ser 355 360 365
- Lys Val Ala Asp Leu Val Glu Gln His Pro Arg Ala Ile Trp Val Ser 370 375 380
- Thr Leu Ile Val Leu Leu Gly Ala Ala Phe Val Pro Thr Leu Lys 385 390 395 400
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- Arg Asp Gly Gln Gln Ala Leu Gly Glu His Phe Pro Gly Gly Ser Gly 420 425 430
- Ser Pro Ala Tyr Ile Ile Val Asp Glu Thr Gln Ala Ala Gln Ala Ala 435 440 445
- Asp Val Val Leu Asn Asn Asp Asn Phe Glu Thr Val Thr Val Thr Ser 450 455 460
- Ala Asp Ser Pro Ser Gly Ser Ala Pro Ile Thr Ala Asp Gly Ile Val 465 470 475 480
- Pro Leu Gly Ser Gly Thr Ala Pro Gly Pro Val Val Val Glu Gly Gln 485 490 495
- Val Leu Leu Gln Ala Thr Leu Val Glu Ala Pro Asp Ser Glu Glu Ala 500 505 510
- Gln Lys Ala Ile Arg Ser Ile Arg Gln Thr Phe Ala Asp Glu Asn Ile

515 520 525

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Leu Leu Val Val Thr Thr Val Val Ser Phe Ala Thr Ala Leu Gly Val 580 585 590

Ala Ala Leu Leu Phe Asn His Val Phe Ser Phe Pro Gly Ala Asp Pro 595 600 605

Ala Val Pro Leu Tyr Gly Phe Val Phe Leu Val Ala Leu Gly Ile Asp 610 615 620

Tyr Asn Ile Phe Leu Val Thr Arg Ile Arg Glu Glu Thr Lys Thr His 625 630 635 640

Gly Thr Arg Leu Gly Ile Leu Arg Gly Leu Thr Val Thr Gly Gly Val 645 650 655

Ile Thr Ser Ala Gly Val Val Leu Ala Ala Thr Phe Ala Ala Leu Tyr 660 665 670

Val Ile Pro Ile Leu Phe Leu Ala Gln Ile Ala Phe Ile Val Ala Phe 675 680 685

Gly Val Leu Ile Asp Thr Leu Leu Val Arg Ala Phe Leu Val Pro Ala 690 695 700

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act Thi	ggo Gly	c gc y Al 3	a As	t ga n As	t ct p Le	g gad u Gli	g cca u Pro 40	o Lys	g gaa s Glu	a tto 1 Lei	g gc ı Al	t gad a Gli 4!	ı Ar	t cto	g cgc u Arg	144
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act Thr 65	Ala	g gg	t tci y Sei	t gco	g gti a Val	l Val	a tto l Phe	gcg Ala	ggt Gly	aco Thr 75	Th	g gto r Val	g cto Lei	g ato u Ile	gct Ala 80	240
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cgc Arg	aac Asn 210	gcg Ala	ccc Pro	atg Met	att Ile	gcg Ala 215	ctt Leu	atc Ile	gac Asp	gca Ala	acc Thr 220	gac Asp	gtc Val	cct Pro	gag Glu	672
gaa Glu 225	gaa Glu	cgc Arg	cca Pro	Leu	gtg Val 230	ttt Phe	gga Gly	cag Gln	Ala	gtg Val 235	gag Glu	caa Gln	ttc Phe	ttg Leu	aac Asn 240	720
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gca Ala	e cc	t ct b Le 27	u Ar	a ct g Le	c tce u Se	g caa r Glr	a cto 1 Let 280	ı Phe	c gte e Va	g ca l Gl:	g at n Me	g ct t Le 28	u Ar	a cct g Pro	tcg Ser	864
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45

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48

96

acc Thi	e ato Met	Pre	g tto Dei	g gct ı Ala	get Ala	cgt Arg 55	J Ala	g cat a His	gce s Ala	g ato a Met	g gga : Gly 60	y Met	g gct : Ala	gto Val	g ggc l Gly	192
act Thr 65	Ala	g ggt a Gly	t tct y Sei	gcg Ala	gtt Val	Va]	tto Phe	gcg Ala	g ggt a Gly	acc 7 Thi 75	Thi	g gto c Val	g ctg Lev	ato Ile	gct Ala 80	240
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Thr Met Pro Leu Ala Ala Arg Ala His Ala Met Gly Met Ala Val Gly 50 55 60

Thr Ala Gly Ser Ala Val Val Phe Ala Gly Thr Thr Val Leu Ile Ala 65 70 75 80

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Ile Ala Ala Ile Thr Val Ala Ile Ala Val Leu Val Ala Leu Ser 100 105 110

Phe Leu Pro Ala Leu Leu Gly Leu Leu Gly Thr Arg Ile Phe Ala Ala 115 120 125

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Met Gly Leu Lys Trp Val Arg Leu Val Arg Lys Met Pro Val Ala Tyr 145 150 155 160

Leu Leu Val Gly Val Val Leu Leu Gly Ala Ile Ala Ile Pro Ala Thr 165 170 175

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Ala Pro Arg Thr Gly Tyr Asp Met Thr Ala Asp Ala Phe Gly Pro Gly 195 200 205

Arg Asn Ala Pro Met Ile Ala Leu Ile Asp Ala Thr Asp Val Pro Glu 210 215 220

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			ttc Phe													835
			ggt Gly													883
	_		gaa Glu 265		-	_			_	_	_	_	-	-	-	931
		-	gcg Ala				_						_		_	979
	_		gcg Ala	_			-		-			-	_		_	1027
_	•		gca Ala							-			-	-	-	1075
-	_		acg Thr		_	_	-	_		-	_	_		-		1123
	-		tgg Trp 345	-	_	_	_		_	_		-	-	_	-	1171
	Asp		att Ile			Arg					Ala					1219

		a Va					l Va					ı Ala			gtg Val	1267
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Pro	gct Alá	a Ası	c gad n Asp	aco Thi 410	: Arc	g gto g Val	gco Alá	caa a Glr	gaç Glu 415	Arg	tto Phe	gac Asp	gag Glu	gcg Ala 420	ttt Phe	1363
Pro	gco Ala	tto Phe	e Arg	Thi	gaç Glu	g ccg	gto Val	aag Lys 430	Leu	gtg Val	gto Val	acc Thr	ggg Gly 435	Ala	gac Asp.	1411
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Gly	Gly	Thr	cca Pro 505	Ala	Met	Glu	Ile	Glu 510	Ser	Ile	Glu	Ala	Leu 515	Phe	Glu	1651
Lys	Leu	Leu 520		Met	Ala	Leu	Tyr 525	Ile	Val	Leu	Ala	Thr 530	Phe	Ile	Leu	1699
atg Met	gca Ala 535	ttg Leu	gta Val	ttt Phe	ggt Gly	tcg Ser 540	gtg Val	att Ile	ttg Leu	ccg Pro	gcg Ala 545	aag Lys	gcc Ala	atc Ile	atc Ile	1747
atg Met 550	acc Thr	att Ile	ctg Leu	ggt Gly	atg Met 555	ggt Gly	gcc Ala	acc Thr	ttg Leu	ggt Gly 560	att Ile	ctc Leu	acc Thr	ttg Leu	atg Met 565	1795
ttc Phe	gtc Val	gat Asp	ggc Gly	gtg Val 570	ggt Gly	gcc Ala	agc Ser	gca Ala	ttg Leu 575	aac Asn	ttc Phe	tcc Ser	cct Pro	ggc Gly 580	cca Pro	1843
ctg Leu	atg Met	agt Ser	cca Pro 585	gtg Val	ctg Leu	gtg Val	Leu	atc Ile 590	atg Met	gct Ala	att Ile	att Ile	tac Tyr 595	gga Gly	ctt Leu	1891
tcc	acc	gac	tat	gag	gtg	ttc	ctg	gta	tct	cgc	atg	gtg	gag	gcc	cgc	1939

Ser Thr Asp Tyr Glu Val Phe Leu Val Ser Arg Met Val Glu Ala Arg 605 gat aaa ggc gaa too acc gac gac gcc atc aga tac ggc act gca cac 1987 Asp Lys Gly Glu Ser Thr Asp Asp Ala Ile Arg Tyr Gly Thr Ala His 620 acc gga tot atc atc acc gcg gcc gca ctg atc atg att gtg gtc tgt 2035 Thr Gly Ser Ile Ile Thr Ala Ala Ala Leu Ile Met Ile Val Val Cys 640 gga gcg ttt ggt ttc tct gag atc gtc atg atg aag tac atc gcg ttc 2083 Gly Ala Phe Gly Phe Ser Glu Ile Val Met Met Lys Tyr Ile Ala Phe 650 655 ggc atg atc gca gcg ctg att ctg gat gcc acc atc atc cgc atg ctg 2131 Gly Met Ile Ala Ala Leu Ile Leu Asp Ala Thr Ile Ile Arg Met Leu 670 ctt gtc ccc cgc cgt gat gca cct gct tcg cga cga caa ctg gtg ggc 2179 Leu Val Pro Arg Arg Asp Ala Pro Ala Ser Arg Arg Gln Leu Val Gly 685 acc cgg ctt cgt taaaaaggcc tacaccgtca tgg 2214 Thr Arg Leu Arg 695 <210> 226 <211> 697 <212> PRT <213> Corynebacterium glutamicum <400> 226 Val Phe Ser Lys Trp Gly His Phe Ala Tyr Arg Phe Arg Arg Ile Val Pro Leu Val Val Ile Ala Ala Ile Leu Ala Leu Phe Val Ile Phe Gly Thr Lys Leu Gly Asp Arg Met Ser Gln Glu Gly Trp Asp Asp Pro Gly Ser Ser Ser Thr Ala Ala Ala Arg Ile Glu Leu Glu Thr Phe Gly Arg Asp Asn Asp Gly Asp Val Val Leu Leu Phe Thr Ala Pro Glu Gly Thr Ser Phe Asp Asp Ala Glu Val Phe Ser Ser Ile Ser Gly Tyr Leu Asp 85 Gly Leu Ile Glu Asn Asn Pro Asp Glu Val Ser His Ile Asn Ser Tyr 105 Phe Asp Thr Arg Asn Gln Asn Leu Leu Ser Lys Asp Gly Thr Gln Thr 115 120

Phe Ala Ala Leu Gly Leu Lys Gly Asp Gly Glu Gln Thr Leu Lys Asp 130 135 140

- Phe Arg Glu Ile Glu Asp Gln Leu His Pro Asp Asn Leu Ala Gly Gly 145 150 155 160
- Val Thr Thr Glu Val Ala Gly Ala Thr Ala Val Ala Asp Ala Leu Asp 165 170 175
- Glu Gly Met Ala Gly Asp Ile Ser Arg Ala Glu Val Phe Ala Leu Pro 180 185 190
- Phe Val Ala Ile Leu Leu Leu Ile Val Phe Gly Ser Val Val Ala Ala 195 200 205
- Ala Met Pro Leu Ile Val Gly Ile Leu Ser Ile Leu Gly Ser Leu Gly 210 215 220
- Ile Leu Ala Ile Leu Ala Gly Phe Phe Gln Val Asn Val Phe Ala Gln 225 235 240
- Ser Val Val Thr Leu Leu Gly Leu Gly Leu Ala Ile Asp Tyr Gly Leu 245 250 255
- Phe Met Val Ser Arg Phe Arg Glu Glu Met Asp Lys Gly Thr Pro Val 260 265 270
- Glu Gln Ala Val Ala Thr Thr Ala Thr Ala Gly Lys Thr Val Val 275 280 285
- Phe Ser Ala Ala Met Val Ala Val Ala Leu Ser Gly Leu Phe Val Phe 290 295 300
- Pro Gln Ala Phe Leu Lys Ser Val Ala Phe Gly Ala Ile Ser Ala Val 305 310 315 320
- Gly Leu Ala Ala Leu Met Ser Val Thr Val Leu Pro Ser Leu Phe Ser 325 330 335
- Met Leu Gly Lys Asn Ile Asp Lys Trp Ser Leu Arg Arg Thr Ala Arg 340 345 350
- Thr Ala Arg Arg Leu Glu Asp Thr Ile Trp Tyr Arg Val Pro Ala Trp 355 360 365
- Ala Met Arg His Ala Lys Ala Val Thr Val Gly Val Val Leu Leu Leu 370 375 380
- Leu Ala Leu Thr Val Pro Leu Thr Gly Val Lys Phe Gly Gly Ile Asn 385 390 395 400
- Glu Thr Tyr Leu Pro Pro Ala Asn Asp Thr Arg Val Ala Gln Glu Arg 405 410 415
- Phe Asp Glu Ala Phe Pro Ala Phe Arg Thr Glu Pro Val Lys Leu Val 420 425 430

Val Thr Gly Ala Asp Asn Asn Gln Leu Ile Asp Ile Tyr Val Gln Ala 435 440 445

Asn Glu Val Glu Gly Leu Thr Asp Arg Phe Thr Ala Gly Ala Thr Thr 450 455 460

Asp Asp Gly Thr Thr Val Leu Ser Thr Gly Ile Gln Asp Arg Ser Leu 465 470 475 480

Asn Glu Gln Val Val Glu Gln Leu Arg Ala Ile Ser Val Pro Glu Gly
485 490 495

Val Glu Val Gln Ile Gly Gly Thr Pro Ala Met Glu Ile Glu Ser Ile 500 505 510

Glu Ala Leu Phe Glu Lys Leu Leu Trp Met Ala Leu Tyr Ile Val Leu 515 520 525

Ala Thr Phe Ile Leu Met Ala Leu Val Phe Gly Ser Val Ile Leu Pro 530 535 540

Ala Lys Ala Ile Ile Met Thr Ile Leu Gly Met Gly Ala Thr Leu Gly 545 550 555 560

Ile Leu Thr Leu Met Phe Val Asp Gly Val Gly Ala Ser Ala Leu Asn 565 570 575

Phe Ser Pro Gly Pro Leu Met Ser Pro Val Leu Val Leu Ile Met Ala 580 585 590

Ile Ile Tyr Gly Leu Ser Thr Asp Tyr Glu Val Phe Leu Val Ser Arg 595 600 605

Met Val Glu Ala Arg Asp Lys Gly Glu Ser Thr Asp Asp Ala Ile Arg 610 615 620

Tyr Gly Thr Ala His Thr Gly Ser Ile Ile Thr Ala Ala Ala Leu Ile 625 630 635 640

Met Ile Val Val Cys Gly Ala Phe Gly Phe Ser Glu Ile Val Met Met 645 650 655

Lys Tyr Ile Ala Phe Gly Met Ile Ala Ala Leu Ile Leu Asp Ala Thr 660 665 670

Ile Ile Arg Met Leu Leu Val Pro Arg Arg Asp Ala Pro Ala Ser Arg 675 680 685

Arg Gln Leu Val Gly Thr Arg Leu Arg 690 695

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ggt ctt agt gaa cta cat gag gct cgc acc gag gaa ctg aag gaa aat 691 Gly Leu Ser Glu Leu His Glu Ala Arg Thr Glu Glu Leu Lys Glu Asn 185 190 195

gta ggt gtc ggg gct tagagaaaca aaaaaggctg cta 729 Val Gly Val Gly Ala 200

<210> 228

<211> 202

<212> PRT

<213> Corynebacterium glutamicum

<400> 228

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Phe Gly Ala Thr Val Ala Ile Phe Gln Glu Gly Ala Phe Gly Ile Ile 35 40 45

Asp Asp Pro Gln Pro Leu Leu Ser Phe Leu Pro Ile Met Leu Ile Gly 50 55 60

Leu Val Phe Gly Leu Ala Met Asp Tyr Gln Ile Phe Leu Val Thr Arg 65 70 75 80

Met Arg Glu Gly Phe Thr Lys Gly Lys Thr Ala Gly Asn Ala Thr Ser 85 90 95

Asn Gly Phe Lys His Gly Ala Arg Val Val Thr Ala Ala Ala Leu Ile 100 105 110

Met Val Ser Val Phe Ala Ala Phe Ile Ala Gln Asp Met Ala Phe Ile 115 120 125

Lys Thr Met Gly Phe Ala Leu Ala Val Ala Val Phe Phe Asp Ala Phe 130 135 140

Val Val Arg Met Met Ile Ile Pro Ala Thr Met Phe Leu Leu Asp Asp 145 150 155 160

Lys Ala Trp Trp Leu Pro Lys Trp Leu Asp Lys Ile Leu Pro Asn Val 165 170 175

Asp Val Glu Gly Glu Gly Leu Ser Glu Leu His Glu Ala Arg Thr Glu 180 185 190

Glu Leu Lys Glu Asn Val Gly Val Gly Ala 195 200

<210> 229 <211> 729

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170 175 180

ggt ctt agt gaa cta cat gag gct cgc acc gag gaa ctg aag gaa aat 691 Gly Leu Ser Glu Leu His Glu Ala Arg Thr Glu Glu Leu Lys Glu Asn 185 190 195

gta ggt gtc ggg gct tagagaaaca aaaaaggctg cta 729 Val Gly Val Gly Ala 200

<210> 230

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<212> PRT

<213> Corynebacterium glutamicum

<400> 230

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Phe Gly Ala Thr Val Ala Ile Phe Gln Glu Gly Ala Phe Gly Ile Ile 35 40 45

Asp Asp Pro Gln Pro Leu Leu Ser Phe Leu Pro Ile Met Leu Ile Gly 50 55

Leu Val Phe Gly Leu Ala Met Asp Tyr Gln Ile Phe Leu Val Thr Arg 65 70 75 80

Met Arg Glu Gly Phe Thr Lys Gly Lys Thr Ala Gly Asn Ala Thr Ser 85 90 95

Asn Gly Phe Lys His Gly Ala Arg Val Val Thr Ala Ala Ala Leu Ile 100 105 110

Met Val Ser Val Phe Ala Ala Phe Ile Ala Gln Asp Met Ala Phe Ile 115 120 125

Lys Thr Met Gly Phe Ala Leu Ala Val Ala Val Phe Phe Asp Ala Phe 130 140

Val Val Arg Met Met Ile Ile Pro Ala Thr Met Phe Leu Leu Asp Asp 145 150 155 160

Lys Ala Trp Trp Leu Pro Lys Trp Leu Asp Lys Ile Leu Pro Asn Val 165 170 175

Asp Val Glu Gly Glu Gly Leu Ser Glu Leu His Glu Ala Arg Thr Glu 180 185 190

Glu Leu Lys Glu Asn Val Gly Val Gly Ala 195 200

<2 <2	12>	1605		cter	ium	glut	amic	บฑ								
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	00> : cacg		ccg	acgt	ctt	aaat	cgcc	ac a	cago	gccgi	t gg	tcta	aaac	acca	acaaaa	60
gaç	gttgi	taac	tgt	accg	acc a	attc	gtta	ca g	ttac	gatco	Met				a acc I Thr 5	115
tta Lev	a caq n Glr	g gcg n Ala	g caa a Gli	a gco n Ala 10	a Pro	t acq	g aaa c Lys	a aco	caa Glr 15	n Arg	tgç J Tr	g gct o Ala	tto Phe	cto Leu 20	gcc Ala	163
gtt Val	ato Ile	ago Ser	ggt Gl ₃ 25	/ Gl	cto Lev	ttt Phe	cto Lev	ato Ile 30	e Gl	gta Val	gac Asp	aac Asr	tcg Ser 35	Ile	ctc Leu	211
tac Tyr	acc Thr	gca Ala 40	Leu	cct Pro	ctg Leu	ı Ctç ı Lev	g cgt Arg 45	Glu	cag Glr	g cto Leu	gca Ala	gcc Ala 50	Ser	gaa Glu	acc Thr	259
caa Gln	gcg Ala 55	Leu	tgg Trp	atc Ile	: atc : Ile	aac Asn 60	Ala	tat Tyr	ccc Pro	ctg Leu	ctc Leu 65	Met	gcg Ala	ggc	ctt Leu	307
cgt Arg 70	Leu	ggt Gly	gcc	ggc	act Thr 75	Leu	ggt Gly	gac Asp	aaa Lys	aac Asn 80	ggc Gly	Cac	cgc Arg	cgg Arg	atg Met 85	355
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ttt Phe	gct Ala	cca Pro	act Thr 105	Ala	tgg Trp	Ala	Leu	Val	Ala	gcg Ala	Arg	Ala	ttc Phe 115	Leu	ggc Gly	451
atc Ile	ggt Gly	gcg Ala 120	gca Ala	acg Thr	atg Met	atg Met	cct Pro 125	gca Ala	acc Thr	ttg Leu	gct Ala	ctg Leu 130	atc Ile	cgc Arg	att Ile	499
acg Thr	ttt Phe 135	gag Glu	gat Asp	gag Glu	cgt Arg	gag Glu 140	cgc Arg	aac Asn	act Thr	gca Ala	att Ile 145	ggt Gly	att Ile	tgg Trp	ggt Gly	547
tcc Ser 150	gtg Val	gca Ala	att Ile	ctt Leu	ggc Gly 155	gct Ala	gcg Ala	gca Ala	ggc Gly	ccg Pro 160	atc Ile	att Ile	ggt Gly	ggt Gly	gcg Ala 165	595

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atg ggc gcg ggt gct ggt tcg gta atg tct gtg tct tcc act gcg att

Met Gly Ala Gly Ala Gly Ser Val Met Ser Val Ser Ser Thr Ala Ile

375

380

385

atc ggt tcc gcg ccg gtg cgt aag gct ggc atg gcg tcg tcg atc gaa

1315

gcg act cat act gat ggt ttg ccg ttt ttc atc gcg ggt cta ttc ttc

Ala Thr His Thr Asp Gly Leu Pro Phe Phe Ile Ala Gly Leu Phe Phe

365

360

1219

		-														rc 1/1buu/
Ile 390		, Se	r Al	a Pr	o Va		g Ly	s Al	a Gl	y Me 40		a Se	r Se	r Il	e Glu 405	
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gat Asp	aac Asn	Phe 440	e Se	g gc r Al	g gg a Gl	t gt: y Va:	t cad 1 Hi: 44!	s His	gcç Ala	g att	t gat e Asp	t ggd p Gly 450	/ Asp	gco Ala	g gcg a Ala	1459
cgt Arg	gca Ala 455	Ser	tto Lev	g gad ı Ası	c acc	c gca r Ala 460	a Ty	att Ile	aac Asn	gto Val	tte L Lei 465	ı Ile	att E Ile	gco Ala	cta Leu	1507
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aat Asn	ccg Pro	aag Lys	gga Gly	gco Ala 490	Asr	aat Asn	gcg Ala	cac His	tag	taaa	aaa	gaga	tgat	tc		1602
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Asp	Asn	Ser 35	Ile	Leu	Tyr	Thr	Ala 40	Leu	Pro	Leu	Leu	Arg 45	Glu	Gln	Leu	
Ala	Ala 50	Ser	Glu	Thr	Gln	Ala 55	Leu	Trp	Ile	Ile	Asn 60	Ala	Tyr	Pro	Leu	
Leu 1	Met .	Ala	Gly	Leu	Arg 70	Leu	Gly	Ala	Gly	Thr 75	Leu	Gly	Asp	Lys	Asn 80	
Gly 1	His I	Arg	Arg	Met 85	Phe	Leu	Met	Gly	Leu 90	Ser	Ile	Phe	Gly	Ile 95	Ala	
Ser 1	Leu (Ala 100	Ala	Phe	Ala	Pro	Thr 105	Ala	Trp	Ala	Leu	Val 110	Ala	Ala	

Arg Ala Phe Leu Gly Ile Gly Ala Ala Thr Met Met Pro Ala Thr Leu 115 120 125

- Ala Leu Ile Arg Ile Thr Phe Glu Asp Glu Arg Glu Arg Asn Thr Ala 130 135 140
- Ile Gly Ile Trp Gly Ser Val Ala Ile Leu Gly Ala Ala Ala Gly Pro 145 150 155 160
- Ile Ile Gly Gly Ala Leu Leu Glu Phe Phe Trp Trp Gly Ser Val Phe
 165 170 175
- Leu Ile Asn Val Pro Val Ala Val Ile Ala Leu Ile Ala Thr Leu Phe 180 185 190
- Val Ala Pro Ala Asn Ile Ala Asn Pro Ser Lys His Trp Asp Phe Leu 195 200 205
- Ser Ser Phe Tyr Ala Leu Leu Thr Leu Ala Gly Leu Ile Ile Thr Ile 210 215 220
- Lys Glu Ser Val Asn Thr Ala Arg His Met Pro Leu Leu Gly Ala 225 235 240
- Val Ile Met Leu Ile Ile Gly Ala Val Leu Phe Ser Ser Arg Gln Lys 245 250 255
- Lys Ile Glu Glu Pro Leu Leu Asp Leu Ser Leu Phe Arg Asn Arg Leu 260 265 270
- Phe Leu Gly Gly Val Val Ala Ala Gly Met Ala Met Phe Thr Val Ser 275 280 285
- Gly Leu Glu Met Thr Thr Ser Gln Arg Phe Gln Leu Ser Val Gly Phe 290 295 300
- Thr Pro Leu Glu Ala Gly Leu Leu Met Ile Pro Ala Ala Leu Gly Ser 310 315 320
- Phe Pro Met Ser Ile Ile Gly Gly Ala Asn Leu His Arg Trp Gly Phe 325 330 335
- Lys Pro Leu Ile Ser Gly Gly Phe Ala Ala Thr Ala Val Gly Ile Ala 340 345 350
- Leu Cys Ile Trp Gly Ala Thr His Thr Asp Gly Leu Pro Phe Phe Ile 355 360 365
- Ala Gly Leu Phe Phe Met Gly Ala Gly Ala Gly Ser Val Met Ser Val 370 375 380
- Ser Ser Thr Ala Ile Ile Gly Ser Ala Pro Val Arg Lys Ala Gly Met 385 390 395 400
- Ala Ser Ser Ile Glu Glu Val Ser Tyr Glu Phe Gly Thr Leu Leu Ser 405 410 415

Val Ala Ile Leu Gly Ser Leu Phe Pro Phe Phe Tyr Ser Leu His Ala 425 Pro Ala Glu Val Ala Asp Asn Phe Ser Ala Gly Val His His Ala Ile 440 Asp Gly Asp Ala Ala Arg Ala Ser Leu Asp Thr Ala Tyr Ile Asn Val 455 Leu Ile Ile Ala Leu Val Cys Ala Val Ala Ala Leu Ile Ser Ser 470 Tyr Leu Phe Arg Gly Asn Pro Lys Gly Ala Asn Asn Ala His 485 <210> 233 <211> 1500 <212> DNA <213> Corynebacterium glutamicum <220> <221> CDS <222> (101)..(1477) <223> RXA01666 <400> 233 cgacgcgccc ctccaccttt tcagtagcgt cacgggcgcc aatcctgtat ttttagcagc 60 agtttgaggg tttttgctcc ccatctttag gagacacccc gtg tcc acg ttt cat Val Ser Thr Phe His aaa gtt ttg atc aac acc atg atc tcc aac gtc acc act gga ttt ctg 163 Lys Val Leu Ile Asn Thr Met Ile Ser Asn Val Thr Thr Gly Phe Leu ttc ttt gcc gtg gtg ttt tgg atg tat ctt tcc act ggc aac gtc gca 211 Phe Phe Ala Val Val Phe Trp Met Tyr Leu Ser Thr Gly Asn Val Ala ctg acc ggc atc gtc agt gga att tac atg ggt ttg atc gcc gtt tgt 259 Leu Thr Gly Ile Val Ser Gly Ile Tyr Met Gly Leu Ile Ala Val Cys 45 tcc atc ttt ttc gga acc gtt gtt gat cac aat cgc aag aag tcc gtc 307 Ser Ile Phe Phe Gly Thr Val Val Asp His Asn Arg Lys Lys Ser Val 65 atg ctg ttt tcc agc gtc acc aca ctc gtg ttt tat tgt ctc agt gcc 355 Met Leu Phe Ser Ser Val Thr Thr Leu Val Phe Tyr Cys Leu Ser Ala ctg gtg tgg gtg ttt tgg ctg gag gaa gac ggc ctg agc atc gga aat 403 Leu Val Trp Val Phe Trp Leu Glu Glu Asp Gly Leu Ser Ile Gly Asn

acc Thr	gc Ala	c cto a Leo	g tg u Tr 10	p Va	g tt l Ph	c gt e Va	t tc 1 Se	t tt r Ph	e Il	c cto e Leo	c ato	c gga e Gly	a tc: 7 Se: 11	r Ile	gtg Val	451
gaa Glu	cae His	e ato s Med 120	Ar	c aa g As:	c at n Il	c gca e Ala	a cto a Leo 125	a Se	c ace	c gto r Val	g gto l Vai	c aco l Thi 130	: Le	g ttg u Lei	gtt Val	499
cct Pro	gaa Glu 135	ı Ala	gaa Glu	a cgo a Aro	c ga g As _l	c aaa o Lys 140	s Ala	a aad a Asi	c ggo n Gly	c cto y Lei	g gta 1 Val 145	l Gly	gco Ala	gtg a Val	caa Gln	547
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	•	10 01	70000	•												PC 1/1B00/0
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Val Val Gln Gly Ala Gly Ala Ala Ile Ile Ala Pro Ala Thr Leu Ala 100 105 110

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Ile Asn Val Pro Ile Ala Ala Val Leu Ala Tyr Ile Val His Lys Ala 165 \$170\$ 175

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Ser Ala Asp Tyr Ser Trp Thr Asp Pro Phe Val Leu Ile Ser Leu Val 210 215 220

Leu Gly Ile Ala Val Phe Ile Trp Phe Leu Arg His Glu Ser Ser Ala 225 230 235 240

Lys Glu Pro Leu Pro Leu Gly Leu Phe Lys Asn Arg Arg Asn 245 250 255

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Val Ala Val Ser Thr Pro Ala Leu Gln Ala Asp Met Gly Ala Ser Tyr

aac gag gtc atc tgg gta acc tcg gtg tat ctc ctc act ttc gcg gtg

Asn Glu Val Ile Trp Val Thr Ser Val Tyr Leu Leu Thr Phe Ala Val

60

70

307

355

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- Arg Asn Phe Ser Leu Gly Asn Ile Cys Ile Met Ala Met Gly Phe Thr 290 295 300
- Val Ala Gly Thr Pro Leu Pro Ile Met Leu Tyr Phe Gln Gln Ala His 305 310 315 320

Gly Met Asn Ala Met Glu Ala Gly Phe Met Met Val Pro Gln Ala Leu 325 Met Ala Ala Val Leu Ser Pro Phe Val Gly Lys Leu Val Asp Arg Ser 345 Asn Pro Gly Leu Met Ala Ala Leu Gly Phe Ser Thr Val Ala Val Ser 360 Ile Val Leu Ser Met Val Met Ile Phe Asp Thr Gly Leu Val Trp 375 Ala Leu Val Ser Met Thr Leu Leu Gly Ile Gly Asn Ala Phe Val Trp 395 Ala Pro Asn Ser Thr Ser Thr Met Arg Asp Leu Pro His Lys Phe Met Gly Ala Gly Ser Gly Val Phe Asn Thr Thr Arg Gln Leu Gly Ser Val Ile Gly Ala Ala Ala Ile Gly Ala Val Met Gln Ile Arg Leu Ala Ala Gly Asp Glu Gly Ala Ala Phe Gly Gln Ala Leu Leu Leu Ala Ala Ala Val Leu Val Ile Gly Ile Val Ala Ser Thr Met Ala Gly Lys Asn Ala His Pro Ala Pro Val Lys Pro 485 <210> 239 <211> 1455 <212> DNA <213> Corynebacterium glutamicum <220> <221> CDS <222> (101)..(1432) <223> RXN03064 <400> 239 tggagccttg tcttcctcca gcaatcccac aacggagcag gttgggatcc cgagaaatgt 60 tgtcatcatc ttggctgtat tagtttttac agcctttgtc atg atg ttg aat gag 115 Met Met Leu Asn Glu act act ctg gca gtc gcg ttg ccg tcg atc atg gcg gac ttt gac att Thr Thr Leu Ala Val Ala Leu Pro Ser Ile Met Ala Asp Phe Asp Ile 10 15 gag gcg aat act gcg cag tgg ttg ctc act ggt ttt atg ttg acc atg

Glu	ı Ala	a As	n Th		a Glı	ı Tr	Le:	u Lei 30		r Gl	y Ph	e Met	: Lei 3!		r Met	
gct Ala	t gto a Val	g gt L Va 4	l Le	t cc	a gct o Ala	act Thi	ggt Gl ₃	y Tr	g at	g tte	g ga u Gl	a cgt u Arg 5(g Phe	t acc	act Thr	259
cgt Arc	agt Ser 55	· Vai	g tt: l Phe	t att	t tto e Phe	gco Ala 60	Thr	g gto Val	g gte L Val	c tte l Phe	c cte e Le: 6	u Ile	ggt Gly	act Thi	gtg Val	307
acg Thr 70	Ala	gcq Ala	g tto a Lei	g tot 1 Sei	cct Pro	Thr	ttt Phe	gcg Ala	ati Ile	ato Met 80	Lei	t gca ı Ala	gco Ala	cgc Arg	gtc Val 85	355
gct Ala	cag Gln	gco Ala	g att a Il∈	ggt Gly 90	7 Thr	gct Ala	gtg Val	ato Ile	ato Met	: Pro	g cto Lev	g ctg ı Leu	ato Met	act Thr	gtc Val	403
gcg Ala	atg Met	acc Thr	gtt Val	. Val	cct Pro	cca Pro	gag Glu	cgc Arg 110	Arg	ggc Gly	gco Ala	gtc Val	atg Met 115	Gly	ttg Leu	451
att Ile	gcg Ala	gto Val 120	Val	atg Met	gcc Ala	gtt Val	ggt Gly 125	cct Pro	gct Ala	ctt Leu	gga Gly	cct Pro 130	agt Ser	gtg Val	gct Ala	499
ggt Gly	ttc Phe 135	Val	ctc Leu	agc Ser	ttg Leu	tct Ser 140	tcg Ser	tgg Trp	cac His	gcg Ala	att Ile 145	ttc Phe	tgg Trp	gtc Val	atg Met	547
gtt Val 150	ccg Pro	ttg Leu	gtg Val	ttt Phe	gtg Val 155	gca Ala	agc Ser	ctg Leu	atc Ile	ggt Gly 160	acc Thr	ctg Leu	cgt Arg	ctg Leu	acc Thr 165	595
aac Asn	gtc Val	agt Ser	gag Glu	cct Pro 170	aaa Lys	aag Lys	act Thr	cct Pro	ttg Leu 175	gat Asp	gtt Val	att Ile	tcc Ser	ttc Phe 180	ctg Leu	643
att Ile	tcc Ser	gca Ala	gtg Val 185	gct Ala	ttc Phe	ggt Gly	ggc Gly	ctt Leu 190	gtg Val	tac Tyr	gcc Ala	ttg Leu	agc Ser 195	tcg Ser	att Ile	691
ggc Gly	atc Ile	att Ile 200	ttg Leu	gaa Glu	ggt Gly	gac Asp	aga Arg 205	agc Ser	gct Ala	ttg Leu	gtc Val	gtg Val 210	ttg Leu	gct Ala	gtc Val	739
ggc Gly	atc Ile 215	att Ile	gcg Ala	ttg Leu	gtg Val	gtg Val 220	ttt Phe	gtg Val	tgg Trp	cgc Arg	cag Gln 225	att Ile	gcc Ala	atg Met	ggt Gly	787
aag Lys 230	cag Gln	gat Asp	aag Lys	Ala	ctg Leu 235	ttg Leu	gat Asp	ctg Leu	cgt Arg	ccg Pro 240	ttg Leu	gcg Ala	att Ile	cgt Arg	gag Glu 245	835
tac Tyr	acc Thr	att Ile	ccg Pro	ctg Leu	gtt Val	gtg Val	ctt Leu	ttg Leu	acg Thr	ctg Leu	ttc Phe	ggt Gly	gcg Ala	ctg Leu	ctc Leu	883

250 255 260

ggt Gly	gto Val	ato Met	aat Asr 265	n Thi	a ctg r Leu	ccg Pro	ctc Leu	tac Tyr 270	Leu	g cag g Gln	gga Gly	tcc Ser	ttg Leu 275	Met	gtc Val	931
acc Thr	gcc Ala	ttg Leu 280	ı Val	c gcq L Ala	g ggt a Gly	cta Leu	gtg Val 285	Leu	ttg Leu	cca Pro	ggt Gly	ggt Gly 290	Leu	ttg Leu	gaa Glu	979
ggt Gly	gtg Val 295	Leu	tcg Ser	p cca Pro	ttt Phe	gtg Val 300	Gly	cga Arg	att Ile	tat Tyr	gat Asp 305	Arg	cat His	ggt Gly	cca Pro	1027
cgc Arg 310	Gly	ctc Leu	gtg Val	atc Ile	ggc Gly 315	ggt Gly	atg Met	tca Ser	ctc Leu	gtt Val 320	gtg Val	atc Ile	tcc Ser	ctg Leu	ttt Phe 325	1075
gca Ala	ctg Leu	tcc Ser	acc Thr	gtc Val 330	gat Asp	gag Glu	ttc Phe	gcc Ala	aac Asn 335	gtg Val	tgg Trp	ttc Phe	atc Ile	atc Ile 340	ggc Gly	1123
gta Val	cac His	atc Ile	gtg Val 345	ttc Phe	tcc Ser	atc Ile	ggc	ctt Leu 350	gcg Ala	ctg Leu	ctg Leu	ttc Phe	acc Thr 355	cca Pro	ctg Leu	1171
atg Met	aca Thr	gtc Val 360	gcg Ala	ctc Leu	gca Ala	tcc Ser	gtc Val 365	ccc Pro	gac Asp	aac Asn	atg Met	tac Tyr 370	ggc Gly	cac His	ggc Gly	1219
tcc Ser	gcg Ala 375	atc Ile	ctc Leu	aac Asn	acc Thr	ctc Leu 380	caa Gln	cag Gln	ctc Leu	gcc Ala	ggc Gly 385	gcc Ala	gca Ala	ggc Gly	acc Thr	1267
gcg Ala 390	gtc Val	atg Met	att Ile	gcg Ala	gtt Val 395	tat Tyr	tcc Ser	acc Thr	gtc Val	agc Ser 400	aac Asn	aac Asn	gcg Ala	ctt Leu	atc Ile 405	1315
gac Asp	ggc Gly	gca Ala	acc Thr	caa Gln 410	caa Gln	acc Thr	gcc Ala	Leu	gcc Ala 415	gac Asp	ggc Gly	gcc Ala	aac Asn	tct Ser 420	gca Ala	1363
ttc Phe	ttc Phe	gcc Ala	tca Ser 425	gcg Ala	tgc Cys	gtg Val	Ala	gtg Val 430	ttt Phe	gca Ala	ctg Leu	atc Ile	gtg Val 435	ggc Gly	ttc Phe	1411
	Val				gcc Ala		taag	ctag	gt c	gcat	gatc	a gc	a			1455

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<211> 444

<212> PRT

<213> Corynebacterium glutamicum

<400> 240

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1 5 10 15

- Ala Asp Phe Asp Ile Glu Ala Asn Thr Ala Gln Trp Leu Leu Thr Gly 20 25 30
- Phe Met Leu Thr Met Ala Val Val Leu Pro Ala Thr Gly Trp Met Leu 35 40 45
- Glu Arg Phe Thr Thr Arg Ser Val Phe Ile Phe Ala Thr Val Val Phe 50 55 60
- Leu Ile Gly Thr Val Thr Ala Ala Leu Ser Pro Thr Phe Ala Ile Met 65 70 75 80
- Leu Ala Ala Arg Val Ala Gln Ala Ile Gly Thr Ala Val Ile Met Pro 85 90 95
- Leu Leu Met Thr Val Ala Met Thr Val Val Pro Pro Glu Arg Arg Gly 100 105 110
- Ala Val Met Gly Leu Ile Ala Val Val Met Ala Val Gly Pro Ala Leu 115 120 125
- Gly Pro Ser Val Ala Gly Phe Val Leu Ser Leu Ser Ser Trp His Ala 130 135 140
- Ile Phe Trp Val Met Val Pro Leu Val Phe Val Ala Ser Leu Ile Gly 145 150 155 160
- Thr Leu Arg Leu Thr Asn Val Ser Glu Pro Lys Lys Thr Pro Leu Asp 165 170 175
- Val Ile Ser Phe Leu Ile Ser Ala Val Ala Phe Gly Gly Leu Val Tyr
- Ala Leu Ser Ser Ile Gly Ile Ile Leu Glu Gly Asp Arg Ser Ala Leu 195 200 205
- Val Val Leu Ala Val Gly Ile Ile Ala Leu Val Val Phe Val Trp Arg 210 215 220
- Gln Ile Ala Met Gly Lys Gln Asp Lys Ala Leu Leu Asp Leu Arg Pro 225 230 235 240
- Leu Ala Ile Arg Glu Tyr Thr Ile Pro Leu Val Val Leu Leu Thr Leu 245 250 255
- Phe Gly Ala Leu Leu Gly Val Met Asn Thr Leu Pro Leu Tyr Leu Gln 260 265 270
- Gly Ser Leu Met Val Thr Ala Leu Val Ala Gly Leu Val Leu Pro 275 280 285
- Gly Gly Leu Leu Glu Gly Val Leu Ser Pro Phe Val Gly Arg Ile Tyr 290 295 300

Asp Arg His Gly Pro Arg Gly Leu Val Ile Gly Gly Met Ser Leu Val 310 315 Val Ile Ser Leu Phe Ala Leu Ser Thr Val Asp Glu Phe Ala Asn Val Trp Phe Ile Ile Gly Val His Ile Val Phe Ser Ile Gly Leu Ala Leu 345 Leu Phe Thr Pro Leu Met Thr Val Ala Leu Ala Ser Val Pro Asp Asn 360 Met Tyr Gly His Gly Ser Ala Ile Leu Asn Thr Leu Gln Gln Leu Ala Gly Ala Ala Gly Thr Ala Val Met Ile Ala Val Tyr Ser Thr Val Ser 390 395 Asn Asn Ala Leu Ile Asp Gly Ala Thr Gln Gln Thr Ala Leu Ala Asp 410 Gly Ala Asn Ser Ala Phe Phe Ala Ser Ala Cys Val Ala Val Phe Ala Leu Ile Val Gly Phe Phe Val Lys Arg Pro Ala Arg 435 440 <210> 241 <211> 1093 <212> DNA <213> Corynebacterium glutamicum <220> <221> CDS <222> (101)..(1093) <223> FRXA00565 <400> 241 tggagccttg tcttcctcca gcaatcccac aacggagcag gttgggatcc cgagaaatgt 60 tgtcatcatc ttggctgtat tagtttttac agcctttgtc atg atg ttg aat gag Met Met Leu Asn Glu act act ctg gca gtc gcg ttg ccg tcg atc atg gcg gac ttt gac att 163 Thr Thr Leu Ala Val Ala Leu Pro Ser Ile Met Ala Asp Phe Asp Ile 10 15 gag gcg aat act gcg cag tgg ttg ctc act ggt ttt atg ttg acc atg 211 Glu Ala Asn Thr Ala Gln Trp Leu Leu Thr Gly Phe Met Leu Thr Met gct gtg gtt ctt cca gct act ggt tgg atg ttg gaa cgt ttt acc act 259 Ala Val Val Leu Pro Ala Thr Gly Trp Met Leu Glu Arg Phe Thr Thr 40

		Va]			tto Phe		Thr					Ile			gtg Val	307
_	Āla				cct Pro	Thr		-		_	Leu					355
					acc Thr					Pro						403
	_		-	Val	cct Pro						-					451
		_	Val	_	gcc Ala	_			_				-			499
					ttg Leu											547
_	_	_			gtg Val 155	-	-	_				_	_	-		595
	-	-			aaa Lys	_				-	_				_	643
		_	-	_	ttc Phe						-	_	_	_		691
			_	_	ggt Gly	-	_	-	-	-	-		_	_	gtc Val.	739
				_	gtg Val			-		_	_		_	_		787
_	-	_	_		ctg Leu 235	_	-	_	_	_	_			_		835
					gtt Val											883
					ctg Leu		Leu									931
acc	gcc	ttg	gtc	gcg	ggt	cta	gtg	ctg	ttg	cca	ggt	ggt	ctt	ttg	gaa	979

Thr Ala Leu Val Ala Gly Leu Val Leu Pro Gly Gly Leu Leu Glu 280 285 290

ggt gtg ctg tcg cca ttt gtg ggt cga att tat gat cgt cat ggt cca 1027 Gly Val Leu Ser Pro Phe Val Gly Arg Ile Tyr Asp Arg His Gly Pro 295 300 305

cgc gga ctc gtg atc ggc ggt atg tca ctc gtt gtg atc tcc ctg ttt 1075 Arg Gly Leu Val Ile Gly Gly Met Ser Leu Val Val Ile Ser Leu Phe 310 325

gca ctg tcc acc gtc gat 1093 Ala Leu Ser Thr Val Asp 330

<210> 242

<211> 331

<212> PRT

<213> Corynebacterium glutamicum

<400> 242

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Phe Met Leu Thr Met Ala Val Val Leu Pro Ala Thr Gly Trp Met Leu 35 40 45

Glu Arg Phe Thr Thr Arg Ser Val Phe Ile Phe Ala Thr Val Val Phe
50 55 60

Leu Ile Gly Thr Val Thr Ala Ala Leu Ser Pro Thr Phe Ala Ile Met
65 70 75 80

Leu Ala Ala Arg Val Ala Gln Ala Ile Gly Thr Ala Val Ile Met Pro 85 90 95

Leu Leu Met Thr Val Ala Met Thr Val Val Pro Pro Glu Arg Arg Gly 100 105

Ala Val Met Gly Leu Ile Ala Val Val Met Ala Val Gly Pro Ala Leu 115 120 125

Gly Pro Ser Val Ala Gly Phe Val Leu Ser Leu Ser Ser Trp His Ala 130 . 135 140

Ile Phe Trp Val Met Val Pro Leu Val Phe Val Ala Ser Leu Ile Gly 145 150 155 160

Thr Leu Arg Leu Thr Asn Val Ser Glu Pro Lys Lys Thr Pro Leu Asp 165 170 175

Val Ile Ser Phe Leu Ile Ser Ala Val Ala Phe Gly Gly Leu Val Tyr 180 185 190

Ala Leu Ser Ser Ile Gly Ile Ile Leu Glu Gly Asp Arg Ser Ala Leu 200 Val Val Leu Ala Val Gly Ile Ile Ala Leu Val Val Phe Val Trp Arg 215 Gln Ile Ala Met Gly Lys Gln Asp Lys Ala Leu Leu Asp Leu Arg Pro 235 Leu Ala Ile Arg Glu Tyr Thr Ile Pro Leu Val Val Leu Leu Thr Leu 250 Phe Gly Ala Leu Leu Gly Val Met Asn Thr Leu Pro Leu Tyr Leu Gln 265 Gly Ser Leu Met Val Thr Ala Leu Val Ala Gly Leu Val Leu Leu Pro 280 Gly Gly Leu Leu Glu Gly Val Leu Ser Pro Phe Val Gly Arg Ile Tyr Asp Arg His Gly Pro Arg Gly Leu Val Ile Gly Gly Met Ser Leu Val Val Ile Ser Leu Phe Ala Leu Ser Thr Val Asp 325 <210> 243 <211> 380 <212> DNA <213> Corynebacterium glutamicum <220> <221> CDS <222> (1)..(357) <223> FRXA02878 <400> 243 tgc ctg tcc acc gtc gat gag ttc gcc acg tgt tgg tca tca ttc gcg 48 Cys Leu Ser Thr Val Asp Glu Phe Ala Thr Cys Trp Ser Ser Phe Ala gac aca tog tgg tto toa tog god ott gog otg otg tto acc oca otg Asp Thr Ser Trp Phe Ser Ser Ala Leu Ala Leu Leu Phe Thr Pro Leu 20 25 atg aca gtc gcg ctc gca tcc gtc ccc gac aac atg tac ggc cac ggc 144 Met Thr Val Ala Leu Ala Ser Val Pro Asp Asn Met Tyr Gly His Gly 35 tcc gcg atc ctc aac acc ctc caa cag ctc gcc ggc gcc gca ggc acc 192 Ser Ala Ile Leu Asn Thr Leu Gln Gln Leu Ala Gly Ala Ala Gly Thr 50 gcg gtc atg att gcg gtt tat tcc acc gtc agc aac aac gcg ctt atc 240

Ala Val Met Ile Ala Val Tyr Ser Thr Val Ser Asn Asn Ala Leu Ile
65 70 75 80

gac ggc gca acc caa caa acc gcc ctc gcc gac ggc gcc aac tct gca
Asp Gly Ala Thr Gln Gln Thr Ala Leu Ala Asp Gly Ala Asn Ser Ala
85 90 95

ttc ttc gcc tca gcg tgc gtg gca gtg ttt gca ctg atc gtg ggc ttc 336 Phe Phe Ala Ser Ala Cys Val Ala Val Phe Ala Leu Ile Val Gly Phe 100 105 110

ttt gta aag agg cca gcc cgc taagctaggt cgcatgatca gca 380 Phe Val Lys Arg Pro Ala Arg 115

<210> 244

<211> 119

<212> PRT

<213> Corynebacterium glutamicum

<400> 244

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Asp Thr Ser Trp Phe Ser Ser Ala Leu Ala Leu Leu Phe Thr Pro Leu 20 25 30

Met Thr Val Ala Leu Ala Ser Val Pro Asp Asn Met Tyr Gly His Gly 35 40

Ser Ala Ile Leu Asn Thr Leu Gln Gln Leu Ala Gly Ala Ala Gly Thr 50 55 60

Ala Val Met Ile Ala Val Tyr Ser Thr Val Ser Asn Asn Ala Leu Ile 65 70 75 80

Asp Gly Ala Thr Gln Gln Thr Ala Leu Ala Asp Gly Ala Asn Ser Ala 85 90 95

Phe Phe Ala Ser Ala Cys Val Ala Val Phe Ala Leu Ile Val Gly Phe 100 105 110

Phe Val Lys Arg Pro Ala Arg 115

<210> 245

<211> 1533

<212> DNA

<213> Corynebacterium glutamicum

<220>

<221> CDS

<222> (101)..(1510)

<223> RXA00648

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200 205 210

agi Sei	t gce r Ala 21	a Le	g ac u Th	c at r Il	t gg e Gl	g tt y Le 22	u Ph	c gt e Va	g gc l Al	a gc a Al	g cto a Leo 22!	ı Val	g ati	t tto	g gtg ı Val	787
ggt G1 ₃ 230	Tr	g gg o Gl	c tg y Tr	g tt p Ph	c ga e Gl 23	u Th	c cg	c cad	g aa n Ly	a to s Se. 24	r Pro	t tto Lei	g att	gat Asp	ctg Leu 245	835
cgo	aco Thi	c act	t ati	t cg e Ar- 25	g Ala	g aco	c gto	g tto l Lei	g ato 3 Mei 25	t Th	a aat r Asr	att i Ile	gcg Ala	tco Ser 260	atc Ile	883
cto Lev	ato Ile	ggt Gly	tto Phe 265	e Thi	c ato	g tat Tyr	gga Gly	a ato Met 270	: Asr	t cto	g ato 1 Ile	ctg Leu	Pro 275	Gln	gtc Val	931
atg Met	cag Gln	cto Leu 280	ı Pro	gta Val	a att	cto Leu	ggg Gly 285	/ Tyr	ggt Gly	cta / Lev	a ggc a Gly	cag Gln 290	Ser	atg Met	ctt Leu	979
cag Gln	atg Met 295	Gly	ato Ile	tgo Trp	g cto Leu	ato Ile 300	Pro	, atg Met	ggt Gly	: cta / Leu	ggc Gly 305	Met	atg Met	'ttg Leu	att Ile	1027
Ser 310	Asn	Ala	Gly	Ala	Ala 315	Ile	Ser	Ala	Ala	His 320		Pro	Arg	Val	Thr 325	1075
Leu	Thr	Ile	Ala	Gly 330	Val	Val	Ile	Ala	Val 335	Gly	tat Tyr	Ala	Leu	Thr 340	Ala	1123
Thr	Val	Leu	Phe 345	Thr	Ile	Gly	Asn	Arg 350	Thr	Pro	gga Gly	Gly	Asp 355	Ala	Asp	1171
Asn	Ala	Leu 360	Ile	Leu	Thr	Thr	Leu 365	Val	Leu	Phe	tca Ser	Val 370	Cys	Ser	Leu	1219
Val	Val 375	Gly	Ile	Gly	Ile	Gly 380	Leu	Ala	Phe	Gly	tcc Ser 385	Met	Pro	Ala	Leu	1267
Ile 390	Met	Gly	Ala	Val	Pro 395	Ala	Thr	Glu	Lys	Ala 400	gca Ala	Ala	Asn	Gly	Phe 405	1315
Asn	Ser	Leu	Met	Arg 410	Ser	Leu	Gly	Thr	Thr 415	Gly	tca Ser	Ser	Ala	Val 420	Ile	1363
ggt Gly	gca Ala	Val	ttg Leu 425	gcc Ala	gga Gly	atg Met	atg Met	agt Ser 430	ggc Gly	gga Gly	gta Val	Pro	acc Thr 435	tta Leu	ggg Gly	1411

gga ttc atg acc act ctg atc atc gga tgc tgc gcc gcg ctt gtg gct 1459 Gly Phe Met Thr Thr Leu Ile Ile Gly Cys Cys Ala Ala Leu Val Ala 445 qcq gtc atc tcc tat ttc atc ccc acc aca acc act gtg gtg gaa gca 1507 Ala Val Ile Ser Tyr Phe Ile Pro Thr Thr Thr Val Val Glu Ala 465 aaa taatcccggc agcgactcga cca 1533 470 <210> 246 <211> 470 <212> PRT <213> Corynebacterium glutamicum <400> 246 Val Val Thr Leu Ala Ser Ala Gly Ile Thr Val Ser Leu Ala Gln Thr Leu Val Ile Pro Ile Ile Gly Arg Leu Pro Glu Ile Phe Asn Thr Thr Ala Ala Asn Ala Ser Trp Ile Ile Thr Val Thr Leu Leu Val Gly Ala 40 Val Ala Thr Pro Val Met Gly Arg Leu Ala Asp Met Tyr Gly Lys Lys Lys Met Met Leu Ile Ser Leu Val Pro Phe Ile Leu Gly Ser Val Ile Cys Ala Val Ser Val Asp Leu Ile Pro Met Ile Ile Gly Arg Gly Phe Gln Gly Leu Gly Ser Gly Leu Ile Pro Leu Gly Ile Ser Leu Met His 105 Asp Leu Leu Pro Arg Glu Lys Ala Gly Ser Ala Ile Ala Leu Met Ser Ser Ser Met Gly Ile Gly Gly Ala Leu Gly Leu Pro Leu Ala Ala Ala Ile Ala Gln Phe Ala Ser Trp Arg Val Leu Phe Trp Phe Thr Ala Leu 150 Val Ala Leu Thr Val Gly Ala Val Ile Trp Lys Ala Ile Pro Ala Arg 170 Pro Arg Ile Val Arg Ser Gly Gly Phe Asp Tyr Phe Gly Ala Leu Gly Leu Ala Met Gly Leu Ile Ala Leu Leu Leu Ala Val Ser Lys Gly Ser

195

200

205

Glu Trp Gly Trp Arg Ser Ala Leu Thr Ile Gly Leu Phe Val Ala Ala 210 $$ 215 $$ 220

Leu Val Ile Leu Val Gly Trp Gly Trp Phe Glu Thr Arg Gln Lys Ser 225 230 235 240

Pro Leu Ile Asp Leu Arg Thr Thr Ile Arg Ala Thr Val Leu Met Thr 245 250 255

Asn Ile Ala Ser Ile Leu Ile Gly Phe Thr Met Tyr Gly Met Asn Leu 260 265 270

Ile Leu Pro Gln Val Met Gln Leu Pro Val Ile Leu Gly Tyr Gly Leu 275 280 285

Gly Gln Ser Met Leu Gln Met Gly Ile Trp Leu Ile Pro Met Gly Leu 290 295 300

Gly Met Met Leu Ile Ser Asn Ala Gly Ala Ala Ile Ser Ala Ala His 305 310 315 320

Gly Pro Arg Val Thr Leu Thr Ile Ala Gly Val Val Ile Ala Val Gly 325 330 335

Tyr Ala Leu Thr Ala Thr Val Leu Phe Thr Ile Gly Asn Arg Thr Pro 340 345 350

Gly Gly Asp Ala Asp Asn Ala Leu Ile Leu Thr Thr Leu Val Leu Phe 355 360 365

Ser Val Cys Ser Leu Val Val Gly Ile Gly Ile Gly Leu Ala Phe Gly 370 375 380

Ser Met Pro Ala Leu Ile Met Gly Ala Val Pro Ala Thr Glu Lys Ala 385 390 395 400

Ala Ala Asn Gly Phe Asn Ser Leu Met Arg Ser Leu Gly Thr Thr Gly
405 410 415

Ser Ser Ala Val Ile Gly Ala Val Leu Ala Gly Met Met Ser Gly Gly 420 425 430

Val Pro Thr Leu Gly Gly Phe Met Thr Thr Leu Ile Ile Gly Cys Cys 435 440 445

Ala Ala Leu Val Ala Ala Val Ile Ser Tyr Phe Ile Pro Thr Thr 450 455 460

Thr Val Val Glu Ala Lys 465 470

<210> 247

<211> 1770

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<213> Corynebacterium glutamicum

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		Trp	_		ggt Gly	-	Trp	_		_					739
					gct Ala 220										787
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					ctc Leu										883
	 _			-	atc			-			_		_	_	931
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					gtt Val										1123
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					aag Lys		Gly								1219
					gtc Val 380										1267
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	ttc Phe				Cys					Leu					cag Gln	1363
	tcc Ser					-	_									1411
	ttc Phe	-					-	-			_	_				1459
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	cca Pro															1651
-	aca Thr				_				-		-	-	_	-		1699
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Ser	Lys	Ser	Gly 20	Ala	Pro	Ser	Ala	His 25	Thr	Ser	Ala	Pro	Tyr 30	Gly	Ala	
Ala	Ala	Thr 35	Glu	Glu	Ala	Val	Glu 40	Glu	Lys	Thr	Lys	Gly 45	Arg	Val	Gly	
Phe	Ile 50	Ile .	Ala .	Ala	Leu	Met :	Leu .	Ala	Met	Leu	Leu 60	Ser	Ser	Leu	Gly	

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- Ile Gly Ala Leu Ala Gln Asn Met Thr Thr Leu Ile Val Ala Arg Ala 130 . 135 . 140
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- Thr Ala Asp Val Thr Thr Ala Arg Glu Arg Ala Lys Tyr Met Gly Ile 165 170 175
- Met Gly Ser Val Phe Gly Leu Ser Ser Ile Leu Gly Pro Leu Leu Gly 180 185 190
- Gly Trp Phe Thr Asp Gly Pro Gly Trp Arg Trp Gly Leu Trp Leu Asn 195 200 205
- Val Pro Ile Gly Ile Ile Ala Leu Val Ala Ile Ala Val Leu Leu Lys 210 215 220
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- Gly Gly Asn Glu Tyr Glu Trp Ala Ser Pro Met Ile Ile Gly Leu Phe 260 265 270
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- Pro Thr Gln Ala Gly Leu Met Leu Ile Pro Met Met Ile Gly Leu Ile 340 345 350
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Lys Trp Tyr Pro Phe Ile Gly Met Leu Ile Met Val Leu Ala Leu Val 375 Leu Leu Ser Thr Leu Thr Pro Ser Ala Ser Leu Ala Leu Ile Gly Leu 390 395 Tyr Phe Phe Val Phe Gly Phe Gly Leu Gly Cys Ala Met Gln Ile Leu 410 Val Leu Ile Val Gln Asn Ser Phe Pro Ile Thr Met Val Gly Thr Ala 425 Thr Gly Ser Asn Asn Phe Phe Arg Gln Ile Gly Gly Ala Val Gly Ser 440 Ala Leu Ile Gly Gly Leu Phe Ile Ser Asn Leu Ser Asp Arg Phe Thr Glu Asn Val Pro Ala Ala Val Ala Ser Met Gly Glu Glu Gly Ala Gln 470 Tyr Ala Ser Ala Met Ser Asp Phe Ser Gly Ala Ser Asn Leu Thr Pro 490 His Leu Val Glu Ser Leu Pro Gln Ala Leu Arg Glu Ala Ile Gln Leu 505 Ser Tyr Asn Asp Ala Leu Thr Pro Ile Phe Leu Ala Leu Thr Pro Ile 515 520 Ala Val Val Ala Ala Ile Leu Leu Phe Phe Ile Arg Glu Asp His Leu 530 535 540 Lys Glu Thr His Glu 545 <210> 249 <211> 841 <212> DNA <213> Corynebacterium glutamicum <220> <221> CDS <222> (101)..(841) <223> FRXA01314 <400> 249 gtgaatggca cgacatgcca caaggcacgc aagctgattt ccaagcctgc tgtcgcaaag 60 caattaaaaa tacttttctt cttagaggtg gattttcaga atg aca tca cag gtc Met Thr Ser Gln Val 1 aag ccg gac gac gaa cgt ccg gta aca att tca aaa agt ggt gca Lys Pro Asp Asp Glu Arg Pro Val Thr Thr Ile Ser Lys Ser Gly Ala

20

15

10

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			Glu		acc Thr			Arg					Ile			259
		Leu			ctt Leu		Ser									307
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					gcc Ala			-		_				_		403
					ggt Gly											451
	-		-	_	ttc Phe								_	_	-	499
_		-			ttg Leu			-	-	_	-	_			-	547
					att Ile 155											595
					gca Ala											643
	-				ctt Leu		Pro	_							_	691
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<213> Corynebacterium glutamicum

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Gln Thr Ile Phe Gly Ser Ala Leu Pro Thr Ile Val Gly Glu Leu Gly

Gly Val Asn His Met Thr Trp Val Ile Thr Ala Phe Leu Leu Gly Gln

Thr Ile Ser Leu Pro Ile Phe Gly Lys Leu Gly Asp Gln Phe Gly Arg

Lys Tyr Leu Phe Met Phe Ala Ile Ala Leu Phe Val Val Gly Ser Ile

Ile Gly Ala Leu Ala Gln Asn Met Thr Thr Leu Ile Val Ala Arg Ala 135 140

Leu Gln Gly Ile Ala Gly Gly Gly Leu Met Ile Leu Ser Gln Ala Ile 150 155

Thr Ala Asp Val Thr Thr Ala Arg Glu Arg Ala Lys Tyr Met Gly Ile

Met Gly Ser Val Phe Gly Leu Ser Ser Ile Leu Gly Pro Leu Leu Gly

Gly Trp Phe Thr Asp Gly Pro Gly Trp Arg Trp Gly Leu Trp Leu Asn

Val Pro Ile Gly Ile Ile Ala Leu Val Ala Ile Ala Val Leu Leu Lys 215

Leu Pro Ala Arg Glu Arg Gly Lys Val Ser Val Asp Trp Leu Gly Ser 230 235

Ile Phe Met Ala Ile Ala Thr

245

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				gcc Ala					Gly				Gly		96
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				ctg Leu							Ğİy				192
			-	gtg Val						_		_		_	240
				atc Ile 85											288
	_	_	_	aca Thr		_	_	_	-	-			_		336
				gga Gly											384
				aac Asn											432
				ttc Phe											480
				ctg Leu 165											528

aac gt Asn Va	c ccc l Pro	gca Ala 180	Ala	gtg Val	gct Ala	tcc Ser	atg Met 185	ggt Gly	gaa Glu	gaa Glu	ggc Gly	gca Ala 190	caa Gln	tac Tyr	576
gcc tc Ala Se		Met													624
ctt gt Leu Va 21	LĞlu					-		_	-	-					672
tac aad Tyr Asi 225															720
gta gto Val Va															768
gaa acq Glu Thi		-	taat	tgaca	aca (cgaaa	actto	cc gt	tc						803
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	Leu	Ile	Gly	Gly	Leu 165	Phe	Ile	Ser	Asn	Leu 170	Ser	Asp	Arg	Phe	Thr 175	Glu	
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	Ala	Ser	Ala 195		Ser	Asp	Phe	Ser 200	Gly	Ala	Ser	Asn	Leu 205	Thr	Pro	His	
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	tttt	cato	ccg t	gaag	atca	c ct	caag	gaaa	a cgo	acga	iàta			cac His			115
		-	ccc Pro			_	-		-	-	-		-	_	_	_	163
			ggc Gly														211
			caa Gln 40														259
,	atg	atg	atg	gcc	tcc	ctt (gac	cag	atg	att	ttc	ggc	aca	gcc	ctg	cca	307

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280 285 290

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	Ile					, Ile					Pro				cag Gln 325	1075
_	-				Asn	_		-	_	Gly		_	-		cca Pro	1123
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							Asn						gtg Val 515			1651

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Ala Leu Met Val Ala Met Met Met Ala Ser Leu Asp Gln Met Ile Phe 50 60

Gly Thr Ala Leu Pro Thr Ile Val Gly Glu Leu Gly Gly Val Asp His 65 70 75 80

Met Met Trp Val Ile Thr Ala Tyr Leu Leu Ala Glu Thr Ile Met Leu 85 90 95

Pro Ile Tyr Gly Lys Leu Gly Asp Leu Val Gly Arg Lys Gly Leu Phe 100 105 110

Ile Gly Ala Leu Gly Ile Phe Leu Ile Gly Ser Val Ile Gly Gly Leu 115 120 125

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Gly Gly Gly Leu Met Ile Leu Ser Gln Ala Ile Ile Ala Asp Val 145 150 155 160

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Phe Gly Leu Ser Ala Val Leu Gly Pro Leu Leu Gly Gly Trp Phe Thr 180 185 190

Glu Gly Pro Gly Trp Arg Trp Ala Phe Trp Met Asn Ile Pro Leu Gly 195 200 205

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- Ser Val Lys Phe Arg Trp Asp Tyr Leu Gly Thr Phe Phe Met Ile Val 225 230 235 240
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- Glu Trp Ser Asp Pro Ile Ile Ile Gly Leu Ile Ile Thr Thr Ile Val 260 265 270
- Ala Ala Leu Leu Val Val Val Glu Leu Arg Ala Lys Asp Pro Leu 275 280 285
- Val Pro Met Ser Phe Phe Gln Asn Arg Asn Phe Thr Leu Thr Thr Ile 290 295 300
- Ala Gly Leu Ile Leu Gly Ile Ala Met Phe Gly Ile Ile Gly Tyr Leu 305 310 315 320
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- Thr Gly Ile Arg Ile Ser Asn Thr Gly Lys Tyr Lys Leu Phe Pro Pro 355 360 365
- Ile Gly Met Val Val Thr Phe Val Ala Leu Ile Phe Phe Ala Arg Met 370 380
- Glu Val Ser Thr Thr Leu Trp Gln Ile Gly Ile Tyr Leu Phe Val Leu 385 390 395 400
- Gly Val Gly Leu Gly Leu Ala Met Gln Val Leu Val Leu Ile Val Gln
 405 . 410 415
- Asn Thr Leu Pro Thr Ala Val Val Gly Ser Ala Thr Ala Val Asn Asn 420 425 430
- Phe Phe Arg Gln Ile Gly Ser Ser Leu Gly Ser Ala Leu Val Gly Gly $435 \hspace{1.5cm} 440 \hspace{1.5cm} 445 \hspace{1.5cm}$
- Met Phe Val Gly Asn Leu Gly Thr Leu Met Glu Glu Arg Met Pro Ala 450 455 460
- Ala Met Ala Gln Leu Ser Pro Glu Glu Gln Ala Ala Met Ala Ala Gln 465 470 475 480
- Gly Gly Leu Asp Ser Asn Glu Leu Thr Pro Ala Ile Val Asn Gln Leu
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- Pro Thr Ala Leu His Asp Ala Phe Ala Gly Ser Tyr Asn Asp Ala Leu 500 505 510

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120 125 130

															a ctg / Leu	
	135	5				140)				145	5				
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cgt Arg	ggc Gly	ego Aro	tac Ty	c ato Med 170	t Gly	gto Val	atg Met	ggt Gly	gga Gly 175	/ Val	tto L Phe	gga Gly	cto Leu	tct Ser 180	gca Ala	643
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cgc Arg	tgg Trp	gca Ala 200	Phe	tgg Trp	g atg Met	aac Asn	atc Ile 205	Pro	ctç Leu	gga Gly	ato Ile	atc Ile 210	Ala	atc Ile	ggt Gly	739
gtc Val	gcc Ala 215	Ile	tac	tto Phe	ctg Leu	gac Asp 220	att Ile	cca Pro	aag Lys	aag Lys	agc Ser 225	Val	aag Lys	ttc Phe	cgc Arg	787
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atc Ile	ctg Leu	ttc Phe	acc Thr	acc Thr 250	Trp	ggt Gly	gga Gly	tcc Ser	cag Gln 255	Tyr	gag Glu	tgg Trp	tct Ser	gat Asp 260	cca Pro	883
atc	atc Ile	att Ile	gga Gly 265	ctg Leu	atc Ile	atc Ile	acc Thr	acc Thr 270	atc Ile	gtt Val	gcc Ala	gct Ala	gca Ala 275	ctg Leu	ctg Leu	931
											gtt Val					979
ttc Phe	caa Gln 295	Asn	Arg	Asn	Phe	acg Thr 300	Leu	Thr	Thr	Ile	gca Ala 305	Gly	ctg Leu	atc Ile	ctg Leu	1027
ggt Gly 310	atc Ile	gca Ala	atg Met	ttc Phe	ggc Gly 315	atc Ile	atc Ile	ggc Gly	tac Tyr	ctt Leu 320	ccg Pro	acc Thr	tac Tyr	ctc Leu	cag Gln 325	1075
atg Met	gtc Val	cac His	gga Gly	atc Ile 330	aac Asn	gcc Ala	acc Thr	gaa Glu	gcc Ala 335	ggc Gly	tac Tyr	atg Met	ctg Leu	atc Ile 340	cca Pro	1123
atg Met	atg Met	Val	ggc Gly 345	atg Met	atg Met	ggt Gly	Thr	tcc Ser 350	atc Ile	tgg Trp	act Thr	ggt Gly	atc Ile 355	cgc Arg	atc Ile	1171

tcc aac aca gga aag tac aaa ctc ttc cca cca atc ggc atg gtt 1219 Ser Asn Thr Gly Lys Tyr Lys Leu Phe Pro Pro Ile Gly Met Val Val 365 acc ttc gtg gca ctg atc ttc ttt gcc cga atg gaa gtg tcc acc acc 1267 Thr Phe Val Ala Leu Ile Phe Phe Ala Arg Met Glu Val Ser Thr Thr ctq tqg cag atc gga atc tac ctc ttc 1294 Leu Trp Gln Ile Gly Ile Tyr Leu Phe 395 <210> 256 <211> 398 <212> PRT <213> Corynebacterium glutamicum Met Thr His Glu Thr Ser Val Pro Gly Pro Ala Asp Ala Gln Val Ala Gly Asp Thr Lys Leu Arg Lys Gly Arg Ala Lys Lys Glu Lys Thr Pro Ser Ser Met Thr Pro Glu Gln Gln Lys Lys Val Trp Trp Val Leu Ser Ala Leu Met Val Ala Met Met Ala Ser Leu Asp Gln Met Ile Phe Gly Thr Ala Leu Pro Thr Ile Val Gly Glu Leu Gly Gly Val Asp His Met Met Trp Val Ile Thr Ala Tyr Leu Leu Ala Glu Thr Ile Met Leu 85 Pro Ile Tyr Gly Lys Leu Gly Asp Leu Val Gly Arg Lys Gly Leu Phe 105 Ile Gly Ala Leu Gly Ile Phe Leu Ile Gly Ser Val Ile Gly Gly Leu Ala Gly Asn Met Thr Trp Leu Ile Val Gly Arg Ala Val Gln Gly Ile Gly Gly Gly Leu Met Ile Leu Ser Gln Ala Ile Ile Ala Asp Val Val Pro Ala Arg Glu Arg Gly Arg Tyr Met Gly Val Met Gly Gly Val Phe Gly Leu Ser Ala Val Leu Gly Pro Leu Leu Gly Gly Trp Phe Thr

180

Glu Gly Pro Gly Trp Arg Trp Ala Phe Trp Met Asn Ile Pro Leu Gly

195 200 205

Ile Ile Ala Ile Gly Val Ala Ile Tyr Phe Leu Asp Ile Pro Lys Lys 210 215 220

Ser Val Lys Phe Arg Trp Asp Tyr Leu Gly Thr Phe Phe Met Ile Val 225 230 235 240

Ala Ala Thr Ser Leu Ile Leu Phe Thr Thr Trp Gly Gly Ser Gln Tyr
245 250 255

Glu Trp Ser Asp Pro Ile Ile Ile Gly Leu Ile Ile Thr Thr Ile Val 260 265 270

Ala Ala Leu Leu Val Val Val Glu Leu Arg Ala Lys Asp Pro Leu 275 280 285

Val Pro Met Ser Phe Phe Gln Asn Arg Asn Phe Thr Leu Thr Thr Ile 290 295 300

Ala Gly Leu Ile Leu Gly Ile Ala Met Phe Gly Ile Ile Gly Tyr Leu 305 310 315 320

Pro Thr Tyr Leu Gln Met Val His Gly Ile Asn Ala Thr Glu Ala Gly 325 330 335

Tyr Met Leu Ile Pro Met Met Val Gly Met Met Gly Thr Ser Ile Trp 340 345 350

Thr Gly Ile Arg Ile Ser Asn Thr Gly Lys Tyr Lys Leu Phe Pro Pro 355 360 365

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1 5

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235 240 245

			y Gl			c aco		Ala					Thr		ctc Leu	881
aca Thi	a ato Met 265	Th	c gg r Gl	t gta y Va	a tto l Phe	gcc Ala 270	ı Val	a ato L Met	g aat : Asn	ggt Gly	ctg Leu 275	Leu	Pro	aac Asn	ctt Leu	929
	a Glr					ggt Gly					Ala					977
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		Ser				ctc Leu 350										1169
	Ile					att Ile										1217
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ctg Leu 440	atc Ile	cca Pro	cgc Arg	cca Pro	gaa Glu 445	tca Ser	atc Ile	acc Thr	gat Asp	aca Thr 450	gtg Val	gca Ala	gcc Ala	aaa Lys	gtc Val 455	1457
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agg 1510

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<400> 258

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Leu Phe Ser Leu Phe Leu Pro Arg Trp Gly Asp Leu Ile Gly Arg Arg 50 60

Lys Val Leu Val Gly Met Met Ile Val Thr Gly Ile Gly Cys Val Val 65 70 75 80

Ala Ala Phe Ala Pro Asn Val Thr Ile Leu Phe Leu Gly Arg Leu Ile $85 \hspace{1cm} 90 \hspace{1cm} 95$

Gln Gly Val Ala Gly Pro Thr Val Pro Leu Cys Leu Ile Ile Leu Arg 100 105 110

Gln Gln Val Thr Asn Glu Lys Gln Tyr Ala Leu Leu Gly Ile Val 115 120 125

Thr Ser Val Asn Gly Gly Ile Gly Gly Val Asp Ala Leu Ala Gly Gly 130 135 140

Trp Leu Ala Glu Thr Leu Gly Phe Arg Ser Ile Phe Trp Val Met Ala 145 150 155 160

Ala Phe Cys Ala Val Ala Ala Leu Ala Leu Pro Phe Ser Val Lys Glu 165 170 175

Ser Thr Ala Glu Glu Thr Pro Lys Met Asp Trp Leu Gly Val Leu Pro 180 185 190

Leu Ala Val Ser Ile Gly Ser Leu Leu Met Ala Phe Asn Glu Ala Gly 195 200 205

Lys Leu Gly Ala Ala Asn Trp Ile Leu Val Val Leu Phe Ile Ile 210 215 220

Gly Ile Ala Gly Val Ile Phe Phe Tyr Asn Ile Glu Lys Arg Val Lys 225 235 240

His Pro Leu Val Ser Val Glu Tyr Leu Gly Gln Arg Arg Thr Trp Ala 245 250 255

Leu Leu Ser Thr Leu Leu Thr Met Thr Gly Val Phe Ala Val Met 260 Asn Gly Leu Leu Pro Asn Leu Ala Gln Asp Ala Ala Asn Gly Ala Gly 280 Met Ser Ala Ser Val Val Ser Trp Trp Thr Leu Thr Pro Tyr Ala Leu 295 Ala Gly Leu Val Phe Gly Pro Ile Ala Gly Ile Leu Ala Gly Lys Phe Gly Tyr Lys Ile Val Leu Gln Ile Gly Ile Ala Ala Thr Ile Ile Gly Val Ala Gly Ala Thr Phe Leu Val Gly Ser Thr Ser His Leu Ala Tyr Leu Gly Ile Ser Ile Phe Val Gly Ile Thr Tyr Ala Gly Ile Ala Asn Ile Met Leu Asn Gly Leu Gly Ile Val Leu Ser Pro Ala Asn Asn Gln Gly Tyr Leu Pro Gly Met Asn Ala Gly Ala Phe Asn Leu Gly Ala Gly Ile Ser Phe Ala Ile Leu Phe Ala Val Ser Thr Ala Phe Ser Asp Asn Gly Gly Tyr Ala Ala Gly Met Trp Ala Gly Val Ile Ile Leu Val 420 425 430 Leu Ala Phe Leu Cys Ser Leu Leu Ile Pro Arg Pro Glu Ser Ile Thr Asp Thr Val Ala Ala Lys Val Gln Ala Glu Glu Ala Ala Gln Ala Ala Ser 465 <210> 259 <211> 1470 <212> DNA <213> Corynebacterium glutamicum <220> <221> CDS <222> (101)..(1447) <223> RXA02087

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				Asp					Ala					aag Lys		211
		_	Lei		_	_	_	Asn						tca Ser		259
		Leu					Val							cgc Arg		307
	Āsp	_			-	Arg					Āla		_	gct Ala		355
					Leu	-	_	_		_		_		gaa Glu 100		403
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														cgt Arg		499
														gga Gly		547
														tgg Trp		595
_			-	-			_			-				ttt Phe 180	-	643
														atc Ile		691
														gtt Val		739
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					cca Pro 315											1075
					aag Lys											1123
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					gct Ala											1267
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440

gattttctca cga 1470

445

<210> 260

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<212> PRT

<213> Corynebacterium glutamicum

<400> 260

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Ala Leu Pro Lys Ile Gln Glu Asp Leu Gly Ala Ser Leu Asn Gln Ala 35 40 45

Val Trp Val Ser Ala Val Tyr Leu Leu Thr Phe Ala Val Pro Leu Leu 50 55 60

Ile Thr Gly Arg Leu Gly Asp Arg Tyr Gly Gln Arg Asn Ile Tyr Leu 65 70 75 80

Ala Gly Met Ala Val Phe Thr Leu Ala Ala Leu Ala Cys Val Phe Ala 85 90 95

Pro Ser Ile Glu Trp Leu Ile Ala Ala Arg Ala Val Gln Gly Leu Gly 100 105 110

Gly Ser Leu Leu Asn Pro Gln Pro Leu Ser Ile Ile His Lys Ile Phe 115 120 125

Ala His Asp Arg Arg Gly Ala Ala Thr Gly Val Trp Ser Ala Val Ala 130 135 140

Ser Ser Ala Gly Leu Phe Gly Pro Val Ile Gly Gly Val Leu Val Gly 145 150 155 160

Trp Ile Ser Trp Arg Ala Val Phe Leu Val Tyr Val Pro Leu Gly Leu 165 170 175

Ile Ser Leu Phe Met Val Ala Arg Tyr Val Pro Lys Leu Pro Thr Gly 180 185 190

Thr Ser Lys Ile Asp Trp Leu Ser Gly Ala Val Ser Leu Val Ala Val

Leu Gly Val Val Leu Ala Leu Gln Gln Gly Pro Glu Leu Gly Trp Gly 210 215 220

Thr Leu Ile Trp Val Ser Leu Ala Val Gly Ile Ala Ala Ala Val Leu 225 230 235 240

Phe Ile Trp Met Gln Thr Arg Ser Lys Ala Pro Leu Met Pro Leu Arg

245 250 255

Ile Phe Lys Thr Arg Asn Phe Ala Ile Gly Ala Phe Ser Ile Phe Ser 260 265 270

Leu Gly Phe Thr Val Tyr Ser Val Asn Leu Pro Ile Met Leu Tyr Leu 275 280 285

Gln Thr Ala Gln Gly Met Ser Ser Gln Leu Ala Gly Leu Met Leu Val 290 295 300

Pro Met Gly Ile Ile Ser Val Val Met Ser Pro Val Ile Gly Arg Leu 305 310 315 320

Val Asp Arg Leu Ala Pro Gly Met Ile Ser Lys Ile Gly Phe Gly Ala 325 330 335

Leu Ile Phe Ser Met Ala Leu Met Ala Val Phe Met Ile Ala As
n Leu 340 345 350

Ser Pro Trp Trp Leu Leu Ile Pro Ile Ile Leu Phe Gly Ser Ser Asn 355 360 365

Ala Met Ser Phe Ala Pro Asn Ser Val Ile Ala Leu Arg Asp Val Pro 370 375 380

Gln Asp Leu Val Gly Ser Ala Ser Gly Phe Tyr Asn Thr Ser Arg Gln 385 390 395 400

Val Gly Ala Val Leu Gly Ala Ala Thr Leu Gly Ala Val Met Gln Ile 405 410 415

Gly Val Gly Thr Val Ser Phe Gly Val Ala Met Gly Ala Ala Ile Leu 420 425 430

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<223> RXA02088

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1 5

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				Phe		att Ile										211
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agt Ser	gcg Ala 55	gtg Val	gtg Val	tcc Ser	atc Ile	ttt Phe 60	gcg Ala	ggc Gly	gcc Ala	cgg Arg	ttg Leu 65	ttg Leu	ttt Phe	gcg Ala	ccg Pro	307
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act Thr	ggt Gly	tta Leu	ctc Leu	acc Thr 90	gtg Val	gct Ala	atc Ile	acc Thr	acg Thr 95	ggg Gly	ctt Leu	gtt Val	gcg Ala	ttg Leu 100	gcg Ala	403
						ctg Leu										451
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ccg Pro	gtg Val 135	gag Glu	atc Ile	cgc Arg	ggg Gly	cgg Arg 140	tgt Cys	tcg Ser	tcg Ser	gta Val	tat Tyr 145	gcc Ala	agt Ser	tcg Ser	ttc Phe	547
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						ttc Phe										643
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cgg Arg	aag Lys	gct Ala 200	gat Asp	agc Ser	aat Asn	agt Ser	gtg Val 205	ccg Pro	gcg Ala	ttg Leu	cgc Arg	ttt Phe 210	gct Ala	gag Glu	gca Ala	739
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gca Ala	gct Ala	gca Ala	ttt Phe	agc Ser 250	aat Asn	ggc Gly	gga Gly	gct Ala	att Ile 255	gcg Ala	ggt Gly	ttt Phe	gcc Ala	atg Met 260	gct Ala	883
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ctg Leu 310	atc Ile	acg Thr	gta Val	tct Ser	gcg Ala 315	ttg Leu	gca Ala	ggt Gly	gct Ala	ggt Gly 320	gcg Ala	ggc Gly	ttg Leu	ctt Leu	aat Asn 325	1075
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gtt Val	ggc Gly	ccg Pro 360	att Ile	ctc Leu	gta Val	ggc Gly	atg Met 365	atc Ile	gca Ala	gaa Glu	cag Gln	gca Ala 370	ggc Gly	ttc Phe	caa Gln	1219
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<211> 405

<212> PRT

<213> Corynebacterium glutamicum

<400> 262

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 35 40 45
- Ser Phe Ala Ala Ser Ala Val Val Ser Ile Phe Ala Gly Ala Arg 50 55 60
- Leu Leu Phe Ala Pro Met Ser Gly Ser Leu Ile Asp Lys Ile Gly Ser 65 70 75 80
- Arg Arg Val Tyr Leu Thr Gly Leu Leu Thr Val Ala Ile Thr Thr Gly 85 90 95
- Leu Val Ala Leu Ala Gln Glu Tyr Trp Gln Ile Leu Leu Arg Gly
 100 105 110
- Ile Ala Gly Ile Gly Ser Thr Met Phe Thr Val Ser Ala Met Gly Leu 115 120 125
- Ile Val Lys Met Ala Pro Val Glu Ile Arg Gly Arg Cys Ser Ser Val 130 135 140
- Tyr Ala Ser Ser Phe Leu Phe Gly Asn Ile Ile Gly Pro Val Val Gly 145 150 155 160
- Ala Ala Met Ser Gly Leu Gly Met Arg Trp Pro Phe Ala Ile Tyr Gly
 165 170 175
- Ala Ser Val Gly Leu Ala Ala Leu Val Val Trp Trp Arg Met Pro Lys 180 185 190
- Thr Asn Asp Ser Leu Arg Lys Ala Asp Ser Asn Ser Val Pro Ala Leu 195 200 205
- Arg Phe Ala Glu Ala Ile Lys Asp Ser Ala Tyr Arg Ser Ala Leu Phe 210 215 220
- Ser Ala Phe Ala Asn Gly Trp Ser Asn Phe Gly Val Arg Val Ala Val 225 230 235 240
- Leu Pro Leu Phe Ala Ala Ala Ala Phe Ser Asn Gly Gly Ala Ile Ala 245 250 255
- Gly Phe Ala Met Ala Ala Phe Ala Ala Gly Asn Ala Leu Cys Leu Gln 260 265 270
- Phe Ala Gly Asp Leu Ser Asp Arg Ile Gly Arg Lys Pro Met Ile Ile 275 280 285
- Ser Gly Leu Ile Val Asn Ala Val Phe Thr Ala Met Ile Gly Phe Gly 290 295 300
- Thr Glu Val Trp Ile Leu Ile Thr Val Ser Ala Leu Ala Gly Ala Gly 305 310 315 320

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Val	. Ile	e Ası	n Gl	y Let 90		u Gly	y Sei	r Ala	95 95		/ Asp	Phe	e Arç	100	Leu	
				o Ala					Pro					Asn	gtg Val	451
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		Val		g ttg ı Lev			Lys					Thr				547
	Thr			g ggt Gly		Asp					Trp					595
			Gly	att Ile	Asp					Ala						643
				ttt Phe												691
			Trp	gtg Val												739
				agc Ser												787
				tcg Ser												835
				aat Asn 250	Pro											883
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cac His	ctg Leu	att Ile 280	ggc Gly	gtg Val	ggg Gly	cat His	ggt Gly 285	cgg Arg	aag Lys	ttg Leu	gag Glu	aag Lys 290	ttg Leu	atc Ile	gct Ala	979
aag Lys	cgc Arg 295	acc Thr	att Ile	gct Ala	ttt Phe	gat Asp 300	gat Asp	gcg Ala	gag Glu	aaa Lys	gta Val 305	acg Thr	ctc Leu	acg Thr	tgc Cys	1027
				cgt Arg												1075

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ccg aag acg cat ccg aca ccg ccg atc atg aat tgg gct gtc cat tt Pro Lys Thr His Pro Thr Pro Pro Ile Met Asn Trp Ala Val His Le 345 350 355	
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Glu Ala Arg Phe Thr His Tyr Gly Gly His Ala Glu Glu Met Val Al 50 55 60	.a
Gly Leu Thr Val Asp Asp Phe Asp Val Ile Ile Pro Ala Gly Gly As 65 70 75 8	sp 10
Gly Thr Val Asn Glu Val Ile Asn Gly Leu Leu Gly Ser Ala Glu Gl 85 90 95	У
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Gly Ser Ala Asn Val Phe Ala Arg Ala Leu Gly Tyr Pro Thr Asp Pr 115 120 125	0
Tyr Ala Ala Ala Asp Ala Leu Val Glu Leu Ile Arg Lys Asn His Th 130 135 140	r
Arg Thr Ile Thr Leu Gly Thr Trp Lys Gly Asp Asp Gln Gly Thr Ar 145 150 155 16	
Trp Phe Ala Val Asn Ala Gly Phe Gly Ile Asp Ala Asp Val Ile Al. 165 170 175	a
Arg Val Glu Arg Ala Arg Ser Phe Gly Phe Ala Ala Ser Pro Leu Le	u

180 185 190

Tyr Leu Gln Val Ser Leu Arg Ala Trp Val Lys Thr Gln Ile Lys Pro 195 200 205

Pro Lys Ile Thr Val Glu Ala Val Asp Ser Lys Gly His Lys Leu Gln 210 215 220

Lys Glu Glu Val Pro Met Leu Leu Ala Ser Asn Thr Asn Pro Trp Thr 225 230 235 240

Phe Leu Gly Pro Leu Pro Val Val Thr Asn Pro Gln Asn Ser Phe Asp 245 250 255

Thr Gly Leu Gly Leu Phe Gly Leu Thr Ser Val Arg Gly Phe Gly Gly 260 265 270

Val Ala Ala Met Met His Leu Ile Gly Val Gly His Gly Arg Lys Leu 275 280 285

Glu Lys Leu Ile Ala Lys Arg Thr Ile Ala Phe Asp Asp Ala Glu Lys 290 295 300

Val Thr Leu Thr Cys Asp Ser Asp Gln Arg Phe Gln Val Asp Gly Glu 305 310 315 320

Tyr Glu Gly Lys Pro Thr Lys Val Val Leu Glu Ser Ile Thr Asp Ala 325 330 335

Val Arg Val Tyr Ala Pro Lys Thr His Pro Thr Pro Pro Ile Met Asn 340 345 350

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ctc gtg ctg ttg ctc gtg ttc cgg tcc att tgg gtc cca ttg atc gcg 163

Leu Val Leu Leu Val Phe Arg Ser Ile Trp Val Pro Leu Ile Ala 10 15 get etg gge ttt gge ttg tea gtt etg get ace ttt ggt get ace gtg 211 Ala Leu Gly Phe Gly Leu Ser Val Leu Ala Thr Phe Gly Ala Thr Val qcq atc ttc caa gaa ggt gct ttc qqc atc atc qac gat cct cag cca 259 Ala Ile Phe Gln Glu Gly Ala Phe Gly Ile Ile Asp Asp Pro Gln Pro 45 ctg ctg tgc ttc 271 Leu Leu Cys Phe 55 <210> 266 <211> 57 <212> PRT <213> Corynebacterium glutamicum <400> 266 Leu Val Leu Ala Phe Leu Val Leu Leu Val Phe Arg Ser Ile Trp Val Pro Leu Ile Ala Ala Leu Gly Phe Gly Leu Ser Val Leu Ala Thr 20 25 30 Phe Gly Ala Thr Val Ala Ile Phe Gln Glu Gly Ala Phe Gly Ile Ile Asp Asp Pro Gln Pro Leu Leu Cys Phe 50 <210> 267 <211> 1443 <212> DNA <213> Corynebacterium glutamicum <220> <221> CDS <222> (101)..(1420) <223> RXN01553 <400> 267 atgatgatgt cctcagcaag tccaagcgcc aagccatgct ggaaacaatt ctcgagctga 60 taccaagcca gacttaaatt tctaccttaa agtcttgagc atg act gtt cag gaa Met Thr Val Gln Glu 1 ttc gac cgc gcg acc aaa ccc aca cca aaa ccc cca att gtt tct tgg 163 Phe Asp Arg Ala Thr Lys Pro Thr Pro Lys Pro Pro Ile Val Ser Trp 15 gcg ttt tgg gat tgg ggt tcc gcc tct ttc aac gcg gtc ctc gtg acc 211

Ala	Phe	Trp	Asp 25		Gly	/ Ser	Ala	Ser 30		Asn	Ala	Val	Leu 35		Thr	
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		Ser			aca Thr		Leu									307
					gtt Val 75	Val					Gly					355
					cgc											403
				Phe	tgt Cys											451
					gta Val											499
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					cga Arg 155											595
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					cgc Arg											691
					gtc Val											739
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PCT/IB00/00922

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- Gly Ala Thr Leu Pro Glu Gly Ser Asn Ala Thr Ser Leu Tyr Ser Met 50 60
- Ala Val Ala Ile Ala Gly Val Ile Val Ala Val Val Ala Pro Val Met 65 70 75 80
- Gly Arg Arg Ser Asp Ile Lys Gly Thr Arg Arg Arg Ser Leu Arg Met
 85 90 95
- Trp Thr Leu Val Thr Val Phe Leu Met Phe Cys Leu Phe Thr Val Lys
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- Asn Thr Asp Pro Thr Phe Phe Trp Phe Gly Val Ala Ile Met Ala Ile 115 120 125
- Ala Asn Ile Thr Phe Glu Phe Ala Glu Val Gln Tyr Tyr Ala Gln Leu 130 135 140
- Ser Gln Ile Ser Thr Arg Glu Asn Val Gly Arg Val Ser Gly Phe Gly 145 150 155 160
- Trp Ser Met Gly Tyr Phe Gly Gly Ile Val Leu Leu Leu Val Cys Tyr 165 170 175
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- Pro Ile Glu Asp Gly Met Asn Ile Arg Leu Val Ala Val Leu Ala Ala 195 200 205
- Val Trp Phe Leu Val Ser Ala Ile Pro Ala Leu Leu Arg Val Pro Glu 210 215 220
- Ile Glu Ala Gln Val Ala Ala Glu Asp His Pro Lys Gly Leu Ile Ala225230235240
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- Arg Asn Ser Val Tyr Phe Leu Ile Ala Ala Thr Val Phe Arg Asp Gly 260 265 270
- Leu Ala Gly Val Phe Thr Phe Gly Ala Ile Leu Ala Val Ser Val Tyr 275 280 285
- Gly Leu Ser Ala Gly Asp Val Leu Leu Phe Gly Val Ala Ala Asn Val 290 295 300

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Gly	Pro	Lys	Pro	Ile 325	Ile	Leu	Ile	Ser	Leu 330		Ile	Met	Ile	Ala 335	Asp	
Ala	Ala	Ile	Leu 340	Phe	Phe	Val	Glu	Gly 345	Pro	Thr	Asn	Phe	Trp 350	Ile	Phe	
Gly	Leu	Ile 355		Cys	Ala	Phe	Val 360	Gly	Pro	Ala	Gln	Ser 365	Ala	Ser	Arg	
Ser	Tyr 370	Leu	Thr	Arg	Leu	Ser 375	Pro	Asp	Gly	Gln	Glu 380	Gly	Gln	Leu	Phe	
Gly 385		Tyr	Ala	Thr	Thr 390	Gly	Arg	Ala	Val	Ser 395	Trp	Met	Val	Pro	Ser 400	
Leu	Phe	Gly	Val	Phe 405	Val	Gly	Leu	Thr	Gly 410	Asp	Asp	Arg	Thr	Gly 415	Ile	
Leu	Ala	Ile	Ala 420	Leu	Ile	Leu	Leu	Phe 425	Gly	Ile	Val	Leu	Leu 430	Ser	Met	
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ccta	aagga	igc t	cacc	ttta	c tc	aatg	ctct	gat	gaca	ccg	-			gca Ala		115
														ctt Leu 20		163
		Thr		-	-						_	_	_	ctg Leu		211
	_	-	-			-	-					-		cgc Arg	_	259

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PCT/IB00/00922

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WO 01/00804

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- Val Leu Ser Leu Met Phe Thr Leu Pro Leu Ser Ala Arg Phe Asn Gly
 35 40 45
- Tyr Arg Leu Arg Arg Thr Glu Ile Phe Trp Ala Thr Leu Leu Thr Val $50 \\ 55 \\ 60$
- Ala Val Gly Ile Met Ile Val Leu Gly Arg Pro Leu Pro Gly Asn Pro 65 70 75 80
- His Pro Pro Leu Asp Arg Trp Ile Pro Val Leu Leu Val Gly Val Ala 85 90 95
- Val Met Gly Gly Met Trp Leu Leu Ala Glu Tyr Val Leu Lys Lys Asp 100 105 110
- Lys Ala Leu Ile Leu Gly Leu Val Thr Gly Ala Leu Phe Gly Tyr Val 115 120 125
- Ala Val Met Ser Lys Ala Ala Val Asp Leu Phe Val His Gln Gly Ile 130 $$135\$
- Thr Gly Leu Ile Leu Asn Trp Glu Gly Tyr Gly Leu Ile Leu Thr Ala 145 150 155 160
- Leu Leu Gly Thr Ile Val Gln Gln Tyr Ser Phe Asn Ala Gly Glu Leu 165 170 175
- Gln Lys Ser Leu Pro Ala Met Thr Ile Ala Glu Pro Ile Val Ala Phe 180 185 190
- Ser Leu Gly Tyr Leu Val Leu Gly Glu Lys Phe Gln Val Val Asp Trp 195 . 200 205
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					Val		-		_	Ile		ctg Leu	_		-	883
				Leu					Arg			gcg Ala				931
			Arg									ggc Gly 290				979
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		_			_	_	Gln	-	_	-	-	atg Met	-			1411

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	Pro			ggc		Phe					Ala					1555
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				cgt Arg												1747
	-	_		acc Thr				_		_	_	_	-			1795
	_	-	-	gac Asp 570	-	_	-	-			-		-	-		1843
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				gtc Val												1987
		_	-	att Ile			_	-						-		2035
		_	-	atg Met 650	-		_	Val					-	_	-	2083
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gat																2472
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1				5					10			_	_	15		
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Pro	Ser	Ile 35	Asp	Ala	Thr	Val	Ser 40	Leu	Val	Glu	Asn	Phe 45	Pro	Asp	Gln	
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Glu 65	Gly	Thr	Thr	Leu	Asp 70	Asp	Pro	Gln	Met	Met 75	Thr	Ala	Met	Asp	Ala 80	
Val	Val	Asp	Tyr	Ile 85	Glu	Asp	Asn	Leu	Pro 90	Asp	Phe	Gly	Gly	Gly 95	Glu	٠

MIG	rne	GLY	100		, vai	. GIL	ı vaı	105		ALG	Бец	. GIU	110		Val
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Thr 145		Phe	Asn	ıle	Asp 150		Glu	Ala	Ala	Glu 155		Val	Glu	Gln	L ys 160
His	Arg	Asp	Val	11e		Glu	Ala	Met	Gln 170		Gly	Glu	Asp	Leu 175	Gly
Val	Arg	Val	Glu 180		Gly	Gly	Pro	Ala 185		Gly	Asp	Pro	Ile 190	Gln	Ile
Glu	Thr	Thr 195	Ser	Glu	Ile	Ile	Gly 200	Ile	Gly	Ile	Ala	Phe 205		Val	Leu
Ile	Phe 210		Phe	Gly	Ser	Leu 215		Ala	Ala	Gly	Leu 220	Pro	Leu	Ile	Thr
Ala 225	Val	Ile	Gly	Val	Gly 230	Ile	Gly	Ala	Leu	Ala 235	Ile	Val	Leu	Ala	Thr 240
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Arg	Ala	Glu 275	Tyr	Lys	Arg	Met	Pro 280	Arg	Ala	Asp	Ala	Ala 285	Gly	Met	Ala
Val	Gly 290	Thr	Ala	Gly	Ser	Ala 295	Val	Val	Phe	Ala	Gly 300	Ala	Thr	Val	Ile
Ile 305	Ala	Leu	Val	Ala	Leu 310	Ile	Ile	Ala	Asp	Ile 315	Gly	Phe	Leu	Thr	Ala 320
Met	Gly	Ile	Ser	Ala 325	Ala	Phe	Thr	Val	Phe 330	Val	Ala	Val	Leu	11e 335	Ala
Leu	Thr	Phe	Ile 340	Pro	Ala	Leu	Leu	Gly 345	Val	Phe	Gly	Gly	His 350	Ala	Phe
Lys	Gly	Lys 355	Ile	Pro	Gly	Ile	Gly 360	Gly	Asn	Pro	Thr	Pro 365	Lys	Gln	Thr
Trp	Glu 370	Gln	Ala	Leu	Asn	Arg 375	Arg	Ser	Lys	Gly	Arg 380	Ser	Trp	Val	Lys
Leu 385	Val	Gln	Lys		Pro	Gly	Leu	Val	Val	Ala 395	Val	Val	Val	Leu	Gly 400

Leu Gly Ala Leu Thr Ile Pro Ala Met Asn Leu Gln Leu Ser Leu Pro 405 410 415

- Ser Asp Ser Thr Ser Asn Ile Asp Thr Thr Gln Arg Gln Ser Ala Asp 420 425 430
- Leu Met Ala Glu Gly Phe Gly Ala Gly Val Asn Ala Pro Phe Leu Val 435 440 445
- Ile Val Asp Thr His Glu Val Asn Ala Asp Ser Thr Ala Leu Gln Pro 450 455 460
- Leu Ile Glu Ala Gln Glu Pro Glu Glu Gly Glu Phe Asp Arg Glu Gln 465 470 475 480
- Ala Ala Arg Phe Ala Thr Tyr Met Tyr Val Thr Gln Thr Tyr Asn Ser 485 490 495
- Asn Ile Asp Val Lys Asn Ala Gln Ile Ile Ser Val Asn Asp Asp Phe 500 505 510
- Thr Ala Ala Gln Ile Leu Val Thr Pro Tyr Thr Gly Pro Ala Asp Lys 515 520 525
- Glu Thr Pro Glu Leu Met His Val Leu Arg Ala Gln Glu Ala Gln Ile 530 540
- Glu Asp Val Thr Gly Thr Glu Leu Gly Thr Thr Gly Phe Thr Ala Val 545 550 556
- Gln Leu Asp Ile Thr Glu Gln Leu Glu Asp Ala Met Pro Val Tyr Leu 565 570 575
- Ala Val Val Gly Leu Ala Ile Phe Leu Leu Ile Leu Val Phe Arg 580 585 590
- Ser Leu Leu Val Pro Leu Val Ala Gly Leu Gly Phe Leu Leu Ser Val 595 600 605
- Gly Ala Ala Phe Gly Ala Thr Val Leu Val Trp Gln Glu Gly Phe Gly 610 615 620
- Gly Phe Val Asn Thr Pro Gly Pro Leu Ile Ser Phe Met Pro Ile Phe 625 630 635 . 640
- Leu Ile Gly Val Thr Phe Gly Leu Ala Met Asp Tyr Gln Val Phe Leu 645 650 655
- Val Thr Arg Met Arg Glu His Tyr Thr His His Asn Gly Lys Gly Gln 660 665 670
- Pro Gly Ser Lys Tyr Thr Pro Val Glu Gln Ser Val Ile Glu Gly Phe 675 680 685
- Thr Gln Gly Ser Arg Val Val Thr Ala Ala Ala Leu Ile Met Ile Ala 690 695 700

705	l Ala Ph	e Ile 710	Asp Gl	n Pro	Leu	Pro 715	Phe	Ile	Lys	Ile	Phe 720	
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Trp Met Pr 75		p Leu .	Asp Are		Leu	Pro	Ser	Leu 765	Asp	Ile	Glu	
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aataaggtga	tgtttca	acg att	taggtta				atg	acg	cca		aaa	115
aataaggtga ctt cac cg Leu His Ar	t ttt gca	a gee o	ctt tta	ıc ggi	taggç atg	ggcc ggt	atg Met 1	acg Thr	cca Pro	cag Gln ctg	aaa Lys 5 ctg	
ctt cac cg	t ttt gca g Phe Ala 10 c atg atc	a gcc (a Ala I) tta a	ctt tta Leu Leu aaa tac	gaa Glu agt	atg Met 15	ggt Gly gtg	atg Met 1 acc Thr	acg Thr tgg Trp	cca Pro acc Thr	cag Gln ctg Leu 20	aaa Lys 5 ctg Leu	115
ctt cac cg Leu His Ar	t ttt gca g Phe Ala 10 c atg atc y Met Ile 25 c ggc ggt a Gly Gly	a gcc (a Ala I) . c tta a e Leu I	ctt tta Leu Leu aaa tac Lys Tyr	gaa Glu agt Ser 30	atg Met 15 gga Gly	ggt Gly gtg Val	atg Met 1 acc Thr aca Thr	acg Thr tgg Trp gac Asp	cca Pro acc Thr gcc Ala 35	cag Gln ctg Leu 20 gta Val	aaa Lys 5 ctg Leu acc Thr	115 163
ctt cac cg Leu His Ar atc atc gg Ile Ile Gl cct att gc Pro Ile Al	t ttt gca g Phe Ala 10 c atg atc y Met Ila 25 c ggc ggt a Gly Gly	a gcc ca Ala I) . c tta a e Leu I c atc c / Ile F	ctt tta Leu Leu aaa tac Lys Tyr cac ggo His Gly 45	gaa Glu Ser 30	atg Met 15 gga Gly ggc Gly	ggt Gly gtg Val ttc Phe	atg Met 1 acc Thr aca Thr ctc Leu	acg Thr tgg Trp gac Asp tgt Cys 50	cca Pro acc Thr gcc Ala 35 ttt Phe	cag Gln ctg Leu 20 gta Val gca Ala	aaa Lys 5 ctg Leu acc Thr gcc Ala	115163211
ctt cac cg Leu His Ar atc atc gg Ile Ile Gl cct att gc Pro Ile Al atc acc atc Ile Thr Ile	t ttt gca g Phe Ala 10 c atg atc y Met Ile 25 c ggc ggt a Gly Gly c acc gto e Thr Val	a gcc ca Ala I . tta a a Leu I . atc c . Ile H . tgg a . Trp I	ctt tta Leu Leu aaa tac Lys Tyr cac ggo His Gly 45 atc aat Ile Asn 60	gaa Glu sagt Ser 30 ttt Phe aat Asn	atg Met 15 gga Gly ggc Gly aag Lys	ggt Gly gtg Val ttc Phe tgg Trp	atg Met 1 acc Thr aca Thr ctc Leu aca Thr 65 gct	acg Thr tgg Trp gac Asp tgt Cys 50 ttc Phe	cca Pro acc Thr gcc Ala 35 ttt Phe ccg Pro	cag Gln ctg Leu 20 gta Val gca Ala cag Gln	aaa Lys 5 ctg Leu acc Thr gcc Ala ggt Gly	115163211259

	-	_		Glu	aag Lys				Phe		_	_		_	-	451
					cca Pro			Ser								499
					tct Ser											547
					aac Asn 155				taa	acaa	cag (cctc	cttc	ac		594
atg																597
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	0> 2° Thr		Gln		Leu	His	Arg	Phe		Ala	Leu	Leu	Glu		Gly	
1	_	— 1	_	5	T 1 -	T 1.	61	W- L	10	7	T .	m	0	15	17- 7	
Thr	Trp	Thr	ьеи 20	Leu	Ile	11e	GIÀ	25	11e	ьeu	ьys	Tyr	30	GIÀ	vaı	
Thr	Asp	Ala 35	Val	Thr	Pro	Ile	Ala 40	Gly	Gly	Ile	His	Gly 45	Phe	Gly	Phe	
Leu	Cys 50	Phe	Ala	Ala	Ile	Thr 55	Ile	Thr	Val	Trp	Ile 60	Asn	Asn	Lys	Trp	
Thr 65	Phe	Pro	Gln	Gly	Ile 70	Ala	Gly	Leu	Ile	Val 75	Ser	Val	Ile	Pro	Trp 80	
Ala	Ala	Leu	Pro	Phe 85	Ala	Leu	Trp	Ala	Asp 90	Lys	Lys	Gly	Leu	Val 95	Ala	
Gly	Gly	Trp	Arg 100	Phe	Ser	Asp	Pro	Ser 105	Glu	Lys	Pro	His	Thr 110	Phe	Phe	
Asp	Lys	Ile 115	Leu	Ala	Gln	Leu	Val 120	Arg	His	Pro	Ile	Arg 125	Ser	Ile	Leu	
Ile	Leu 130	Leu	Val	Ile	Ile	Ala 135	Val	Val	Phe	Ser	Ile 140	Leu	Leu	Ala	Met	
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    Val Ile Ile Thr Ala Gly Ile Leu Val Ala Thr Ala Thr Ala Leu
                                         10
cta atg atc acc gcg gtc agc gag tca acg tac atc gtc atc tcc ctc
Leu Met Ile Thr Ala Val Ser Glu Ser Thr Tyr Ile Val Ile Ser Leu
                                     25
gee gge tte tee ett tat gge ett gge ete gga ete tte gee ace eea
                                                                   205
Ala Gly Phe Ser Leu Tyr Gly Leu Gly Leu Gly Leu Phe Ala Thr Pro
gtc acc gat act gcg ctt gga aca ctt ccc aaa gac cgt acc ggc gct
                                                                   253
Val Thr Asp Thr Ala Leu Gly Thr Leu Pro Lys Asp Arg Thr Gly Ala
ggt gca ggt gta ttc aag atg tcc tct tcc ctc ggc gca gca ctc ggc
                                                                   301
Gly Ala Gly Val Phe Lys Met Ser Ser Ser Leu Gly Ala Ala Leu Gly
atc gca atc tcc act tca gtg ttc ctc gca ctt cgc gac ggc acc tcc
                                                                   349
Ile Ala Ile Ser Thr Ser Val Phe Leu Ala Leu Arg Asp Gly Thr Ser
                     85
                                         90
atc aac tcc gac gtc gca ctc gcc gga aca gtt tca ctt ggc atc aac
Ile Asn Ser Asp Val Ala Leu Ala Gly Thr Val Ser Leu Gly Ile Asn
                                    105
gtt gta ttc gca gca aca gcc acc atc acc gca gca gtc ctt att cca
                                                                   445
Val Val Phe Ala Ala Thr Ala Thr Ile Thr Ala Ala Val Leu Ile Pro
                                120
aaa gee get gge aaa gte tea caa ace age ate ace ett eet gag eea
                                                                   493
Lys Ala Ala Gly Lys Val Ser Gln Thr Ser Ile Thr Leu Pro Glu Pro
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Thr Asp Thr Ala Leu Gly Thr Leu Pro Lys Asp Arg Thr Gly Ala Gly 50 55 60

Ala Gly Val Phe Lys Met Ser Ser Leu Gly Ala Ala Leu Gly Ile 65 70 75 80

Ala Ile Ser Thr Ser Val Phe Leu Ala Leu Arg Asp Gly Thr Ser Ile 85 90 95

Asn Ser Asp Val Ala Leu Ala Gly Thr Val Ser Leu Gly Ile Asn Val 100 105 110

Val Phe Ala Ala Thr Ala Thr Ile Thr Ala Ala Val Leu Ile Pro Lys 115 120 125

Ala Ala Gly Lys Val Ser Gln Thr Ser Ile Thr Leu Pro Glu Pro Ala 130 135 140

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att gat gtc ctc gcc gac ccg atc gat ggc acc cca ctt gta ggc gcc 163
Ile Asp Val Leu Ala Asp Pro Ile Asp Gly Thr Pro Leu Val Gly Ala
10 20

gaa gat ttc tca cgg ttg gtg tct gaa tct ggg cat tcc tac gat gtt 211 Glu Asp Phe Ser Arg Leu Val Ser Glu Ser Gly His Ser Tyr Asp Val

25 . 30 35

	cgt Arg															259
tca Ser	ggc Gly 55	gat Asp	gat Asp	gca Ala	cag Gln	atg Met 60	atc Ile	gcg Ala	gat Asp	cgg Arg	gaa Glu 65	acc Thr	ttc Phe	ctt Leu	tct Ser	307
	ggt Gly															355
	gtc Val															403
	gaa Glu															451
	gtt Val															499
	aag Lys 135															547
	gca Ala															586

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Pro Leu Val Gly Ala Glu Asp Phe Ser Arg Leu Val Ser Glu Ser Gly $20 \\ 25 \\ 30$

His Ser Tyr Asp Val Ala Arg Gln Gly Tyr Val Thr Leu Ala Gly Gly 35 40 45

Ala Gly Leu Arg Tyr Ser Gly Asp Asp Ala Gln Met Ile Ala Asp Arg 50 55 60

Glu Thr Phe Leu Ser Gly Gly His Phe Ala Pro Phe Val Glu Ala Val 65 70 75 80

Thr Glu His Val Gln Asp Val Val Asp Gln Ala Gly Leu Ser Asp Asp

85 90 95

Ala Gln Pro Val Val Cys Glu Ile Gly Ala Gly Thr Gly Tyr Tyr Leu 100 105 110

Ser His Thr Leu Asp Ser Val Ala Gly Ser Arg Gly Ile Gly Ile Asp 115 120 125

Val Ser Val His Ala Ala Lys Arg Leu Ala Lys Cys His Pro Arg Val 130 135 140

Ser Ser

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1 5 10

ttt aaa gca tta acg tca tat tta aag aaa cac aat tgt tta tat gtc 96
Phe Lys Ala Leu Thr Ser Tyr Leu Lys Lys His Asn Cys Leu Tyr Val
20 25 30

ctt gta gat cca tat tta att gaa aat tta cgc aat gca gac ggt gaa 144 Leu Val Asp Pro Tyr Leu Ile Glu Asn Leu Arg Asn Ala Asp Gly Glu 35 40

att gtt aaa tct tat gat aac cga gca ttt gtt aga aca atg gat aaa 192 Ile Val Lys Ser Tyr Asp Asn Arg Ala Phe Val Arg Thr Met Asp Lys 50 60

tta ggt tat aaa cac caa ggt ttc cct gta ggt tat gat tca atg agc $$ 240 Leu Gly Tyr Lys His Gln Gly Phe Pro Val Gly Tyr Asp Ser Met Ser $$ 65 $$ 75 $$ 80

caa atc cgt tgg ctg tca gtg tta gat tta aaa gat aag act gaa gac 288 Gln Ile Arg Trp Leu Ser Val Leu Asp Leu Lys Asp Lys Thr Glu Asp 85 90 95

caa ctt tta aaa gaa atg gat tat caa acg aga cgt aat att aaa aaa $\,$ 336 Gln Leu Leu Lys Glu Met Asp Tyr Gln Thr Arg Arg Asn Ile Lys Lys $\,$ 100 $\,$ 105 $\,$ 110

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		_	att Ile		_		_	_		_	_	384
			ttc Phe									432
			gag Glu									480
			atg Met									528
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<213> Corynebacterium glutamicum

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Leu Val Asp Pro Tyr Leu Ile Glu Asn Leu Arg Asn Ala Asp Gly Glu

Ile Val Lys Ser Tyr Asp Asn Arg Ala Phe Val Arg Thr Met Asp Lys

Leu Gly Tyr Lys His Gln Gly Phe Pro Val Gly Tyr Asp Ser Met Ser

Gln Ile Arg Trp Leu Ser Val Leu Asp Leu Lys Asp Lys Thr Glu Asp

Gln Leu Leu Lys Glu Met Asp Tyr Gln Thr Arg Arg Asn Ile Lys Lys

Thr Tyr Asp Ile Gly Val Lys Thr Lys Thr Leu Thr Ile Asp Glu Thr 120

Gln Thr Phe Phe Asp Leu Phe His Met Ala Glu Glu Lys His Gly Phe 135 140

Lys Phe Arg Glu Leu Pro Tyr Phe Glu Glu Met Gln Lys Leu Tyr Asp 150 155

Asp His Ala Met Leu Lys Leu Ala Tyr Ile Asp Leu Asn Glu Tyr Leu 165 170 175

Lys Thr Leu Gln Leu 180

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	l Val					n Val					ı Glr				ggt Gly 165	595
					a Val					Ala					gtg Val	643
gtç Val	g cag . Glm	Gly Gly	ttg Leu 185	Arç	a att	tto Lei	aag Lys	ggt Gly 190	Let	g ggd i Gly	c gcg / Ala	att Ile	gtc Val	. Thr	gtg Val	691
			Tyr					Gly					Lys		gtt Val	739
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	Ala					Ala					Ála				gcg Ala 245	835
					Ser					Ile					ctc Leu	883
aca Thr	cag Gln	ttt Phe	ttg Leu 265	atc Ile	atg Met	ccg Pro	atg Met	acc Thr 270	atg Met	ctt Leu	ggt Gly	cga Arg	aat Asn 275	gtg Val	gca Ala	931
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ctc Leu	ggt Gly 295	gct Ala	gat Asp	ttt Phe	gag Glu	aga Arg 300	gtg Val	tct Ser	gcg Ala	cat His	gat Asp 305	gcg Ala	gac Asp	aag Lys	gct Ala	1027
gag Glu 310	gag Glu	att Ile	atc Ile	caa Gln	caa Gln 315	ctt Leu	gcc Ala	aaa Lys	ggt Gly	ttg Leu 320	acg Thr	gtt Val	att Ile	cga Arg	ggc Gly 325	1075
act Thr	gat Asp	gag Glu	cag Gln	ctc Leu 330	gtt Val	gag Glu	gta Val	tta Leu	gag Glu 335	cag Gln	ttg Leu	cca Pro	cgt Arg	act Thr 340	cgg Arg	1123
gtg Val	att Ile	gtg Val	gct Ala 345	cct Pro	cat His	gcg Ala	Ala	gat Asp 350	ctt Leu	ttt Phe	gat Asp	caa Gln	agt Ser 355	gtc Val	agg Arg	1171
gac Asp	aat Asn	gtg Val	cat His	ccc Pro	gtg Val	gca Ala	gag Glu	gtc Val	gcg Ala	gag Glu	aaa Lys	gcc Ala	att Ile	gaa Glu	gtt Val	1219

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Leu Gln Arg Leu Trp Phe Trp Ile Ala Met Leu Ala Val Leu Phe Leu 35 40 45

Thr Ala Met Thr Val Asn Trp Ile Ala Arg Tyr Met Leu Val Arg Ser 50 60

Gln Gln Leu Val Ser His Asp Leu Arg Met Leu Val Thr Asp Arg Ile 65 70 75 80

Gln Asp Pro Arg Gly Phe Ala Gly Lys Glu Arg Thr Ala Gly Gly Leu 85 90 95

Leu Ser Ile Ala Ser Ser Asp Thr Gln Arg Val Gly Asp Ile Val Met 100 105 110

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Val	Val 130	Met	Tyr	Ser	Ile	Asn 135	Pro	Trp	Leu	Ser	Val 140	Ala	Val	Leu	Ile
Gly 145	Gly	Pro	Leu	Leu	Val 150	Val	Val	Ala	Ile	Gln 155	Val	Ser	Lys	Pro	Leu 160
Gln	Lys	Arg	Ser	Gly 165	Ala	Arg	Gln	Gln	Ala 170	Val	Ala	Gln	Ala	Ala 175	Ala
Thr	Ala	Thr	Asp 180	Val	Val	Gln	Gly	Leu 185	Arg	Ile	Leu	Lys	Gly 190	Leu	Gly
Ala	Ile	Val 195	Thr	Val	Arg	Arg	Arg 200	Tyr	Glu	Ala	Ile	Ser 205	Gly	Glu	Ala
Tyr	Arg 210	Lys	Thr	Val	His	Ala 215	Asp	Ala	Ala	Glu	Ala 220	Arg	Leu	Asn	Gly
Val 225	Thr	Asp	Ala	Ala	Gly 230	Ala	Ile	Phe	Val	Ser 235	Ala	Leu	Gly	Ile	Gly 240
Ala	Gly	Phe	Leu	Ala 245	Leu	Gln	Gly	Gln	Met 250	Ser	Ile	Gly	Asp	Leu 255	Ile
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•		275			Ser		280					285			
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				325	Thr				330					335	
			340		Val			345					350		
Asp	Gln	Ser 355	Val	Arg	Asp	Asn	Val 360	His	Pro	Val	Ala	Glu 365	Val	Ala	Glu
Lys	Ala 370	Ile	Glu	Val	Ala	Ser 375	Cys	Asp	Asp	Ile	Pro 380	Gly	Gly	Ser	Ser
Lys 385	Ile	Val	Gly	Glu	Gly 390	Gly	Arg	Leu	Leu	Ser 395	Gly	Gly	Gln	Arg	Gln 400
Arg	Val	Ala	Leu	Ala 405	Arg	Ala	Ile	Ala	Phe 410	Asp	Pro	Glu	Val	Leu 415	Val

Leu Gln Asp Pro Thr Thr Ala Val Asp Ser Val Thr Glu Gln Asn Ile Ala Gln Gln Val Ala Ala His Arg Ala Gly Lys Val Thr Ile Val Phe 440 Ser Glu Ala Pro Ala Trp Ser Ala Val Ala Asp Gln His Val Glu Ala 455 Ala Ala Leu Arg Glu Val Met Lys 470 <210> 283 <211> 1470 <212> DNA <213> Corynebacterium glutamicum <220> <221> CDS <222> (101)...(1447) <223> RXN01190 <400> 283 cagggttttg atgagaacaa cacacaccgc ttcaagcatt ctgcgaagaa tgatcaggcg 60 gcagcggggc aaggttgcgt ttggcgcatt ctttttgggg atg tgg cag ctg tcg Met Trp Gln Leu Ser gaa gca ttg gtg ccg att gcg att ggt ttg atc gtt gat cat gcg gtt 163 Glu Ala Leu Val Pro Ile Ala Ile Gly Leu Ile Val Asp His Ala Val 10 ctc aca aaa gat ctc cgc cga tta gtg gtc ggg ctt gtc gct ttt gtt 211 Leu Thr Lys Asp Leu Arg Arg Leu Val Val Gly Leu Val Ala Phe Val 259 gtg ctg ttt gtg gtg ttg agt ttt tct aat cgt ttc ggt tcg cgc gcg Val Leu Phe Val Val Leu Ser Phe Ser Asn Arg Phe Gly Ser Arg Ala 45 307 ttq aat agg gcc gtg aac ttt gaa tcc cat gcg ctc cgc gta gag gta Leu Asn Arq Ala Val Asn Phe Glu Ser His Ala Leu Arg Val Glu Val 60 gcc gat cat gcg ttg aag aat ctg gat ccg cgc aat ttg gtg cct ggc 355 Ala Asp His Ala Leu Lys Asn Leu Asp Pro Arg Asn Leu Val Pro Gly 403 gag gtg atg tcg cgg tcc acc gca gat gcg gat tct tcg acg cgt att Glu Val Met Ser Arg Ser Thr Ala Asp Ala Asp Ser Ser Thr Arg Ile ttc ggg cag atc gga acc ggt gtt tcg gct gcg acg gga ttt ctt ggt 451 Phe Gly Gln Ile Gly Thr Gly Val Ser Ala Ala Thr Gly Phe Leu Gly

105 110 115

		acc Thr 120	Tyr					Asp							499
		ctg Leu													547
		tct Ser				Val					Lys				595
		cag Gln			Asp										643
		ggc Gly		Arg											691
		gcg Ala 200													739
		att Ile													787
_		gct Ala				_		-			_			 _	835
_		gca Ala								Leu			_	-	883
		agc Ser													931
		gtg Val 280													979
_	_	agc Ser	-				-		_			-			1027
	-	agc Ser	_					-			_	-			1075
		gac Asp													1123

				Val	cca Pro											1171
			Ile		gag Glu											1219
_		Ser			tcg Ser		Gly	-	-	_	_		-	_	-	1267
	Ala	_		_	gac Asp 395		_	_	-		_	-	-		acc Thr 405	1315
					gtg Val											1363
					aaa Lys											1411
			_		gat Asp						_	taat	ttga	atg		1457
qca	tcate	ana d														1470
9.0	coac.	ogu (Jac													1470
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100 105 110

Thr Gly Phe Leu Gly Ala Ala Thr Tyr Leu Leu Ile Ser Asp Trp Leu 115 120 125

- Val Gly Leu Leu Val Leu Val Leu Val Pro Ile Ile Ser Gly Val Val 130 135 140
- Ala Leu Ala Ser Lys Gly Ile Ser Lys Arg Ser Val Thr Gln Glu 145 150 155 160
- Lys Leu Ala Glu Ser Gly Ala Gln Ala Ser Asp Ile Met Met Gly Leu 165 170 175
- Arg Val Ile Lys Ala Ile Gly Gly Glu Arg Trp Ala Val Lys Thr Phe 180 185 190
- Glu Lys Ala Ser Gln Ala Ser Ala Arg Ala Ala Val Asp Thr Ala Val 195 200 205
- Ala Ser Gly Lys Val Ala Gly Ile Gly Glu Leu Ser Ile Ala Val Asn 210 215 220
- Leu Ala Ala Val Leu Leu Leu Ala Gly Trp Arg Val Thr Thr Gly Glu 225 230 235 240
- Leu Gly Pro Gly Gln Leu Ile Ala Ile Val Gly Val Ala Val Tyr Leu 245 250 255
- Ser Glu Pro Ile Arg Leu Leu Ser Asn Ser Ile Asn Ala Ser Ala Ile 260 265 270
- Ala His Gly Ala Ala Glu Arg Val Ala Asn Phe Leu Asn Leu Asp Glu 275 280 285
- Ser Gln Ala Gln Tyr Glu Ser Ser Glu Thr Ile Asn Asp Gly Glu Phe 290 295 300
- Leu Val Ile Val Pro Pro Ala Ser Thr Leu Pro His Gly Asp Asn Ile 305 310 315 320
- Leu Ala Thr Pro His Ala Ala Asp Ile Phe Glu Gly Thr Leu Arg Ser 325 330 335
- Asn Ile Ser Met Asn His Glu Asp Asn Val Pro Ile Asp Pro Gln Val 340 345 350
- Ile Arg Ala Ser Gly Leu Thr Asp Ile Ile Glu Val Asp Gly Leu Asp 355 360 365
- Ala Pro Val Arg Asp Thr Gly Ser Asn Leu Ser Gly Gly Gln Arg Gln 370 375 380
- Arg Val Ala Leu Ala Arg Ala Leu His Ala Asp Ala Glu Val Leu Val 385 390 395 400
- Leu Met Asp Pro Thr Ser Ala Val Asp Ser Val Thr Glu Val Ser Ile

405 410 415

Ala Gln Gly Ile Lys Gln Leu Arg Ala Gly Lys Thr Thr Ile Val Val

Ser Ser Ser Pro Ala Phe Tyr Asn Leu Ala Asp Arg Val Ile Ser His 440

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cca att cca gtg ctg gta gtg tcc gca ctt cga gga att ggg ttc ggt

Pro Ile Pro Val Leu Val Val Ser Ala Leu Arg Gly Ile Gly Phe Gly

gcg ctc acc gtc gca gaa tct gcg ttg gtg gct gaa ctc gtt ccc gta

Ala Leu Thr Val Ala Glu Ser Ala Leu Val Ala Glu Leu Val Pro Val

110

105

95

163

211

259

307

355

403

451

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	cc caa er Glr 135	Met					Āla					Gly				547
	gc tad y Tyr 0					· Val					Ile					595
	g gto a Val				ı Arg					Lys					Gln	643
	a cca n Pro			Ser					Ser							691
_	g ctg l Leu	_	Pro		_	-	-	Thr	-	_		_				739
	a gtg a Val 215	Ser					Ala									787
	a ggt u Gly O															835
	a atg r Met															883
_	g cct l Pro			-	-			_	-			,,,				931
_	c gtt l Val				-											979
	g att u Ile 295															1027
	c gaa n Glu)															1075
	gaa Glu		Ser													1123
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PCT/IB00/00922

WO 01/00804

Ile Gly Ser Phe Leu Leu Gly Ile Val Ala Ala Ser Leu Ala Tyr Ser 345 350 ggt gct ttt ggt tcc gga gcc gtg gtg att ttg ttt gga atc gtt ttg 1219 Gly Ala Phe Gly Ser Gly Ala Val Val Ile Leu Phe Gly Ile Val Leu 365 acc acc gcc gat cga atc att ggg cgg cac cgc att act gaa tac aac 1267 Thr Thr Ala Asp Arg Ile Ile Gly Arg His Arg Ile Thr Glu Tyr Asn 380 aac acc cgc gcg cgt ttg cgc cag gtg cca gtc gct cgg cgt gca gtg 1315 Asn Thr Arg Ala Arg Leu Arg Gln Val Pro Val Ala Arg Arg Ala Val 395 400 caa ggg ctg cgc aac agg cgc aaa gat cgc taaaacgctt ttcgacgcca 1365 Gln Gly Leu Arg Asn Arg Arg Lys Asp Arg 410 ccc 1368

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<212> PRT

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<400> 286

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Ala Val Ala Gly Ala Thr Thr Gly Ile Phe Met Ala Ala Thr Val Ile 35 40 45

Thr Gln Ile Phe Thr Pro Ala Ala Leu Arg Lys Ile Gly Tyr Thr Pro 50 55 60

Val Met Ala Phe Ala Ala Phe Met Leu Gly Val Pro Ala Ile Gly Tyr 65 70 75 80

Ile Phe Ser Val Glu Pro Ile Pro Val Leu Val Val Ser Ala Leu Arg 85 90 95

Gly Ile Gly Phe Gly Ala Leu Thr Val Ala Glu Ser Ala Leu Val Ala 100 105 110

Glu Leu Val Pro Val Arg Phe Leu Gly Lys Ala Ser Gly Met Leu Gly 115 120 125

Val Phe Ile Gly Leu Ser Gln Met Leu Phe Leu Pro Ala Gly Leu Ala 130 135 140

Leu Gly Asp Gln Phe Gly Tyr Asn Val Val Tyr Val Leu Gly Ala Val 145 150 155 160

Ile Ala Leu Val Ala Ala Val Met Cys Leu Arg Ile Pro Gln Val Lys 165 170 175

Ala Ala Ala Lys Gln Gln Pro Gln Val Ser Glu Gln Glu Arg Ser Val 180 185 190

Ser Thr Trp Lys Leu Val Leu Val Pro Ser Leu Ala Val Thr Ser Leu 195 200 205

Ser Met Thr Phe Gly Ala Val Ser Ser Phe Leu Pro Ala Ala Val Ile 210 215 220

Glu Leu Asp Pro Gly Leu Gly Ala Ala Leu Ala Gly Ile Ile Leu Ser 225 230 235 240

Ile Thr Gly Gly Ser Ser Met Val Phe Arg Tyr Leu Ser Gly Val Ile 245 250 255

Ala Asp Arg Arg Gly Val Pro Gly Thr Thr Met Ile Pro Ala Gln Ile 260 265 270

Ile Gly Phe Leu Gly Val Val Leu Ile Thr Val Thr Ile Phe Gln Gly 275 280 285

Trp Ser Val Trp Leu Leu Ile Ile Gly Ala Val Met Phe Gly Gly Ala 290 295 300

Phe Gly Met Val Gln Asn Glu Ala Leu Leu Ser Met Phe Phe Arg Leu 305 310 315 320

Pro Arg Thr Arg Val Ser Glu Ala Ser Ala Ile Trp Asn Ile Ala Phe 325 330 335

Asp Ser Gly Thr Gly Ile Gly Ser Phe Leu Leu Gly Ile Val Ala Ala 340 345 350

Ser Leu Ala Tyr Ser Gly Ala Phe Gly Ser Gly Ala Val Val Ile Leu 355 360 365

Phe Gly Ile Val Leu Thr Thr Ala Asp Arg Ile Ile Gly Arg His Arg 370 375 380

Ile Thr Glu Tyr Asn Asn Thr Arg Ala Arg Leu Arg Gln Val Pro Val 385 390 395 400

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Met Ala Ser Ser Ile

1 5

aac atc gga gtg ttc aac ctt gga aat gct gtt gct gcc tgg ctt gct 163 Asn Ile Gly Val Phe Asn Leu Gly Asn Ala Val Ala Ala Trp Leu Ala 10 15 20

ggt gca acc atc acc act tcc ctt gga ctc aca tca gcc gga tta gtt 211 Gly Ala Thr Ile Thr Thr Ser Leu Gly Leu Thr Ser Ala Gly Leu Val
25 30 35

ggc ggt ttg atg acg tcc ctc gga cta gtg ttg gcc atc gtg gct gtg 259 Gly Gly Leu Met Thr Ser Leu Gly Leu Val Leu Ala Ile Val Ala Val
40 45 50

gtt ttg cgt cga aaa gcg caa ggc acc caa gcg acc atc agc gtt gtg 307 Val Leu Arg Arg Lys Ala Gln Gly Thr Gln Ala Thr Ile Ser Val Val 55 60 65

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<211> 75

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Ser Ala Gly Leu Val Gly Gly Leu Met Thr Ser Leu Gly Leu Val Leu 35 40 45

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		Ser Arg (act gtg ctg gaa Thr Val Leu Glu	787
				ggt gga tat gat Gly Gly Tyr Asp 245	835
		Val Leu A		gcc cgt gac caa Ala Arg Asp Gln 260	883
3 2 0	Ala Glu Lys			gca cgt gct cga Ala Arg Ala Arg 275	931
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-	_	Arg Lys I		gcg gaa tcc agt Ala Glu Ser Ser	1027
	-			cgc atc gct cgg Arg Ile Ala Arg 325	1075
		Arg Lys G		ctg cag ttc agc Leu Gln Phe Ser . 340	1123
				acg ttg aat gat Thr Leu Asn Asp 355	1171
gca agc ttc acc Ala Ser Phe Thr 360				gta tcc atc caa Val Ser Ile Gln 370	1219
gta aat gct ggc Val Asn Ala Gly 375					1267
aaa too aca ttg Lys Ser Thr Leu 390					1315
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			gtg cgc aca ctg Val Arg Thr Leu 450	
		His Val Glu	cgg gac gtc gaa Arg Asp Val Glu 465	
			gcg ctg cta cag Ala Leu Leu Gln 480	
			acc aac cac ctt Thr Asn His Leu	
	Gln Leu Glu		gcc tcg tat gat Ala Ser Tyr Asp 515	
			ttg gac gct gtg Leu Asp Ala Val 530	
		Ala Gly Glu	gtt agg gag cta Val Arg Glu Leu 545	1741
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Pro Ala Asp Ala Phe Val Gly Tyr Leu Pro Gln Glu His Thr Arg Thr

Ile Leu Ala Gly Val Glu Lys Pro Leu Ala Gly Thr Ile Ala Leu Ser 50 60

Val Gly Val Val Gly Val Asn Gly Ala Gly Lys Ser Thr Phe Leu Lys

65 70 75 80

Ser Gly Glu Thr Ile Ala Val Tyr Ile Ala Arg Arg Thr Gly Cys Gln 85 90 95

Ala Ala Thr Thr Ala Met Asp Asp Thr Ala Glu Ala Phe Gly Ala Asp 100 105 110

Pro Asp Asn Ala Ala Leu Ala Asp Ala Tyr Ala Glu Ala Leu Asp Arg 115 120 125

Trp Met Ala Ser Gly Ala Ala Asp Leu Asp Glu Arg Ile Pro Ile Val 130 135 140

Leu Ala Asp Leu Gly Phe Glu Leu Pro Thr Ser Thr Leu Met Glu Gly 145 150 155 160

Leu Ser Gly Gly Gln Ala Ala Arg Val Gly Leu Ala Ala Leu Leu Leu 165 170 175

Ser Arg Phe Asp Ile Val Leu Leu Asp Glu Pro Thr Asn Asp Leu Asp 180 185 190

Leu Asp Gly Leu Glu Gln Leu Glu Asn Phe Val Gln Gly Leu Arg Gly 195 200 205

Gly Val Val Leu Val Ser His Asp Arg Glu Phe Leu Ser Arg Cys Val 210 215 220

Thr Thr Val Leu Glu Leu Asp Leu His Gln Asn Ser His His Val Tyr 225 230 235 240

Gly Gly Gly Tyr Asp Ser Tyr Leu Glu Glu Arg Ala Val Leu Arg Gln 245 250 255

His Ala Arg Asp Gln Tyr Glu Glu Phe Ala Glu Lys Lys Lys Asp Leu 260 265 270

Val Ala Arg Ala Arg Thr Gln Arg Glu Trp Ser Ser His Gly Val Arg 275 280 285

Asn Ala Ile Lys Arg Ala Pro Asp Asn Asp Lys Leu Arg Lys Lys Ala 290 295 300

Ala Ala Glu Ser Ser Glu Lys Gln Ala Gln Lys Val Arg Gln Met Glu 305 310 315 320

Ser Arg Ile Ala Arg Leu Glu Glu Val Glu Glu Pro Arg Lys Glu Trp 325 330 335

Lys Leu Gln Phe Ser Val Gly Lys Ala Ser Arg Ser Ser Ser Val Val 340 345 350

Ser Thr Leu Asn Asp Ala Ser Phe Thr Gln Gly Asp Phe Thr Leu Gly 355 360 365

Pro Val Ser Ile Gln Val Asn Ala Gly Asp Arg Ile Gly Ile Thr Gly

370 375 380 Pro Asn Gly Ala Gly Lys Ser Thr Leu Leu Arg Gly Leu Leu Gly Asn Gln Glu Pro Thr Ser Gly Thr Ala Thr Met Gly Thr Ser Val Ala Ile Gly Glu Ile Asp Gln Ala Arg Ala Leu Leu Asp Pro Gln Leu Pro Leu 425 Ile Ser Ala Phe Glu Lys His Val Pro Asp Leu Pro Ile Ser Glu Val 440 Arg Thr Leu Leu Ala Lys Phe Gly Leu Asn Asp Asn His Val Glu Arg Asp Val Glu Lys Leu Ser Pro Gly Glu Arg Thr Arg Ala Gly Leu Ala Leu Leu Gln Val Arg Gly Val Asn Val Leu Val Leu Asp Glu Pro Thr Asn His Leu Asp Leu Glu Ala Ile Glu Gln Leu Glu Gln Ala Leu Ala Ser Tyr Asp Gly Val Leu Leu Leu Val Thr His Asp Arg Arg Met Leu 520 Asp Ala Val Gln Thr Asn Arg Arg Trp His Val Glu Ala Gly Glu Val 535 530 Arg Glu Leu 545 <210> 291 <211> 1638 <212> DNA <213> Corynebacterium glutamicum

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ccc gcg cca gca acc gtc aac gcg gta ttc aac agc aac ggc ttc 163 Pro Ala Pro Ala Thr Val Asn Ala Val Phe Asn Asn Ser Asn Gly Phe 10 15

ati	t gco	c tc	c at r Me 2	t Le	g gg u Gl	c aad y Asr	c cag n Glr	g gto n Val	L Va	c aad l Asi	c act	t gti r Val	gte L Val	l Glu	g acc u Thr	211
ato Met	g gad : Asp	c according to the term of the	r Gl	a tte u Phe	c ggo e Gl	c gto y Val	e ego L Arg 45	, Ile	: gtg • Val	g gat L Asp	aad Asi	ato n Met 50	Le	gto u Vai	ggt LGly	259
tto Phe	tce Ser 55	Thi	c tto	g ggo ı Gl	c gad y Asp	ggc Gly 60	/ Met	aac Asn	caa Glr	a gco a Ala	gco Ala 65	a Glu	a ggt a Gly	gco Ala	act Thr	307
acq Thr 70	Leu	ago Ser	c gat c Asp	ggo Gl	gto Val 75	. Gly	tcc Ser	gcc Ala	aac Asn	gac Asp 80	Gly	gca Ala	gtt Val	caç Glr	t ctt Leu 85	355
gcc Ala	gac Asp	ggc Gly	gcg Ala	gto Val 90	. Thr	ctg Leu	cgc Arg	gac Asp	ggc Gly 95	Ile	gca Ala	agt Ser	gcc Ala	aat Asn 100	gag Glu	403
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ctg Leu	tct Ser 135	gcg Ala	ggc Gly	acc Thr	gcc Ala	caa Gln 140	cta Leu	ggc Gly	caa Gln	ggc Gly	gca Ala 145	acc Thr	cag Gln	gtt Val	tca Ser	547
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Asn Met Leu Val Gly Phe Ser Thr Leu Gly Asp Gly Met Asn Gln Ala 50 55 60

Ala Glu Gly Ala Thr Thr Leu Ser Asp Gly Val Gly Ser Ala Asn Asp 65 70 75 80

Gly Ala Val Gln Leu Ala Asp Gly Ala Val Thr Leu Arg Asp Gly Ile 85 90 95

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Pro Leu Thr Ala Tyr Val Pro Asp Ile Asn Ser Gln Leu Ile Thr Leu 165 170 175

Arg Asp Gly Ala Ala Thr Ile Ala Ser Glu Leu Ser Asp Pro Ser Ser 180 185 190

Thr Tyr Arg Ser Gly Val Asp Ser Ala Val Ser Ala Ser Gln Gln Leu 195 200 205

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210 215 220

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Ser Gln Val Pro Thr Phe Ala Asp Gly Ala Asp Thr Thr Ile Ala Thr 275 280 285

Pro Val Glu Thr Glu Gln Ala Gly Asp Thr Thr Pro Leu Phe Gly Ile 290 295 300

Gly Leu Ala Pro Phe Phe Met Ala Val Gly Leu Phe Met Gly Ala Thr 305 310 315 320

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Arg Met Gly Gly Phe Arg Gly Thr Leu Ala Ser Tyr Leu Pro Ser Thr 340 345 350

Val Leu Gly Leu Gly Gln Ala Thr Ile Met Trp Ala Val Leu Tyr Phe 355 360 365

Leu Leu Asp Leu Asn Pro Ala His Pro Ala Gly Leu Trp Met Ala Met 370 375 380

Val Ala Ile Ser Trp Val Phe Ile Ser Ile Thr His Met Phe Asn Asn 385 390 395 400

Val Ala Gly Pro Ser Ala Gly Arg Val Leu Ser Ile Val Met Met Ser 405 410 415

Phe Gln Leu Val Ser Ser Gly Gly Leu Tyr Pro Pro Glu Thr Gln Pro 420 425 430

Ala Phe Phe His Trp Phe His Thr Tyr Asp Pro Ile Thr Tyr Ala Val 435 440 445

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His Val Phe Gly Ala Gln Ser Asn Ala Lys Ser Ala Asp Gln Gln Val 115 : 120 125

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Lys Gly Val Leu Asp Gly Val Ala Leu Gly Leu Pro Ala Leu Met Arg 145 150 155 160

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Leu	Asp	Gly 35	Val	Glu	Asn	Ala	Glu 40	Val	Lys	Phe	Ser	Ser 45	Gly	Arg	Ile	
Leu	Ile 50	Thr	His	Asp	Pro	Gln 55	Lys	Val	Ser	Val	Arg 60	Asp	Leu	Val	Thr	

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His Leu Ala Asp Ile Val Asp Lys Ser Pro Ala Ala Val Ser Gln His 50 55 60

Leu Ala Arg Leu Arg Met Ala Arg Ile Val Ser Thr Arg Gln Glu Gly
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Gln Arg Val Phe Tyr Lys Leu Thr Asn Glu His Ala Ser Gln Leu Val 85 90 95

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Pro Pro His His His Arg Glu Arg Glu Gln Ser 115 120

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BGI-124CPPC - 97 -

416

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	1/21, C12Q 1/68, C07K 14/34	

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(22) International Filing Date: 23 June 2000 (23.06.2000)

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199 31 413.6	8 July 1999 (08.07.1999)	DE
199 31 457.8	8 July 1999 (08.07.1999)	DE
199 32 230.9	9 July 1999 (09.07.1999)	DE
199 32 209.0	9 July 1999 (09.07.1999)	DE
199 32 914.1	14 July 1999 (14.07.1999)	DE
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199 41 382.7	31 August 1999 (31.08.1999)	DE

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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: CORYNEBACTERIUM GLUTAMICUM GENES ENCODING STRESS, RESISTANCE AND TOLERANCE PROTEINS

(57) Abstract: Isolated nucleic acid molecules, designated SRT nucleic acid molecules, which encode novel SRT proteins from Corynebucterium glutamicum are described. The invention also provides antisense nucleic acid molecules, recombinant expression vectors containing SRT nucleic acid molecules, and host cells into which the expression vectors have been introduced. The invention still further provides isolated SRT proteins, mutated SRT proteins, fusion proteins, antigenic peptides and methods for the improvement of production of a desired compound from C. glutamicum based on genetic engineering of SRT genes in this organism.

Inte nal Application No PCT/IB 00/00922

A. CLASSIFICATION OF SUBJECT MATTER
1PC 7 C12N15/31 C12N1/21 C12Q1/68 C07K14/34 According to International Patent Classification (IPC) or to both national classification and IPC **B. FIELDS SEARCHED** Minimum documentation searched (classification system followed by classification symbols) CO7K C12N C12Q Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practical, search terms used) EPO-Internal, BIOSIS C. DOCUMENTS CONSIDERED TO BE RELEVANT Citation of document, with indication, where appropriate, of the relevant passages Relevant to claim No. DATABASE EBI [Online] AC X13385, 19 March 1999 (1999-03-19) Х 6,8 BARASH S. ET AL.: "Enterococcus faecalis genome contig" XP002152527 abstract JAEGER WOLFGANG ET AL: "A Corynebacterium X 1,2, 8-19,22 glutamicum gene conferring multidrug resistance in the heterologous host Escherichia coli." JOURNAL OF BACTERIOLOGY, vol. 179, no. 7, 1997, pages 2449-2451, XP002152524 ISSN: 0021-9193 the whole document Further documents are listed in the continuation of box C. Patent family members are listed in annex. Special categories of cited documents: T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the "A" document defining the general state of the art which is not considered to be of particular relevance invention earlier document but published on or after the international "X" document of particula: relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled "O" document referring to an oral disclosure, use, exhibition or document published prior to the international filing date but later than the priority date claimed "&" document member of the same patent family Date of the actual completion of the international search Date of mailing of the international search report 13.02.01 14 November 2000 Name and mailing address of the ISA Authorized officer European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Kania, T Fax: (+31-70) 340-3016

2

Inte: nat Application No PCT/IB 00/00922

		PC1/1B 00/00922
	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to daim No.
X	WEHRMANN AXEL ET AL: "Different modes of diaminopimelate synthesis and their role in cell wall integrity: A study with Corynebacterium glutamicum." JOURNAL OF BACTERIOLOGY, vol. 180, no. 12, June 1998 (1998-06), pages 3159-3165, XP002152525 ISSN: 0021-9193 cited in the application the whole document	1,2,8, 19,22
X	PETER H ET AL: "CORYNEBACTERIUM GLUTAMICUM IS EQUIPPED WITH FOUR SECONDARY CARRIERSFOR COMPATIBLE SOLUTES: IDENTIFICATION, SEQUENCING, AND CHARACTERIZATION OF THE PROLINE/ECTOINE UPTAKE SYSTEM, PROP, AND THE ECTOINE/PROLINE/GLYCINE BETAINE CARRIER, ECTP" JOURNAL OF BACTERIOLOGY, WASHINGTON, DC, US, vol. 180, no. 22, 1998, pages 6005-6012, XP000917352 ISSN: 0021-9193 the whole document	1,2, 8-19,22
X	CHAN MING-SHUN ET AL: "Cloning of m-fluorophenylalanine-resistant gene and mutational analysis of feedback-resistant prephenate dehydratase from Corynebacterium glutamicum." BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, vol. 219, no. 2, 1996, pages 537-542, XP002152526 ISSN: 0006-291X the whole document	1,2, 8-19,22
X	EP 0 752 472 A (AJINOMOTO KK) 8 January 1997 (1997-01-08) the whole document	1,2, 8-19,22, 25-34
X	WO 99 02692 A (YAGOSHI CHIZU ;AJINOMOTO KK JP); KIMURA—EIICHIRO—(JP); NAKAMURA—J) 21 January 1999 (1999-01-21) the whole document & EP 1 002 866 A (AJINOMOTO KK) 24 May 2000 (2000-05-24)	1,2, -8 -19,22, 25-34
x	WO 88 09819 A (MASSACHUSETTS INST TECHNOLOGY) 15 December 1988 (1988-12-15) the whole document	1,2, 8-19,22, 25-34

Inte. nal Application No
PCT/IB 00/00922

		PC1/1B 00/00922
C.(Continu	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	FR 2 607 827 A (PASTEUR INSTITUT) 10 June 1988 (1988-06-10) the whole document	1-38
A	EP 0 252 558 A (SCLAVO SPA) 13 January 1988 (1988-01-13) the whole document	35
P , X	DATABASE EBI [Online] AC AF237667, 14 March 2000 (2000-03-14) KIM H. AND LEE H.: "Nucleotide sequence of the lmrB gene in Corynebacterium glutamicum" XP002152528 abstract	1-24
		·
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2

PCT/IB 00/00922

Box i	Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)						
This Inte	ernational Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:						
1.	Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:						
2.	Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:						
	Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).						
Box II	Observations where unity of invention is lacking (Continuation of item 2 of first sheet)						
This Inter	rnational Searching Authority found multiple inventions in this international application, as follows:						
	see additional sheet						
1.	As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.						
2.	As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.						
3.	As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:						
.4. X	No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-38 partially						
Remark (The additional search fees were accompanied by the applicant's protest. No protest accompanied the payment of additional search fees.						

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: invention 1: claims 1-38 partially

An isolated nucleic acid molecule from Corynebacterium glutamicum encoding a stress, resistance, or tolerance gene disclaiming the F-designated genes in table 1. Said gene having the SEQ ID NO:1, homologs (at least 50% homology), variants, and DNA sequences hybridizing thereto, as well as vectors and host cells comprising said sequences. An isolated stress, resistance, or tolerance polypeptide from C. glutamicum. Said protein having the SEQ ID NO:2, homologs (at least 50% homology), and variants thereof. The use of said sequences to modify the production of or produce a fine chemical from said host cell, the fine chemical especially being an amino acid.A method for diagnosing the presence or activity of Corynebacterium diphtheriae in a subject employing said sequences.A host cell comprising said nucleic acid sequences wherein said sequences are disrupted modified, or under the control of a heterologous regulatory region.

2. Claims: inventions 2-122: claims 1-38 partially

as invention 1 but relating to the pairs of sequences as listed in Table 1 (apart from the ones disclaimed)

...formation on patent family members

Inte. nal Application No PCT/IB 00/00922

		· · · · · · · · · · · · · · · · · · ·			00,00322
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